CLINICAL MEDICINE

Vol. 58 *NOVEMBER, 1951* *No. ~~10~~ 11*

CLINICAL MEDICINE

ESTABLISHED 1894

Published Monthly by the

AMERICAN JOURNAL OF CLINICAL MEDICINE, INC.
1232-36 CENTRAL AVENUE, WILMETTE, ILLINOIS

FREDERIC R. STEARNS, M.D.
Editor

C. W. HOTZE
Publisher

NICAL MEDICINE, published monthly by the Amer- Journal of Clinical Medicine, Inc. Title registered U.S. Patent Office. Entered as second class matter ust 1, 1942, at the Post Office at Wilmette, Illinois, er Act of March 3, 1879.

NUSCRIPTS should be addressed to The Editor, *ical Medicine*, 1405 Eden Court, Topeka, Kansas. nuscripts accepted only with the explicit understanding y they are contributed exclusively for publiation in *ical Medicine*.

SCRIPTION PRICES United States and possessions Canada, 1 year 5.00, 2 years 8.00, 3 years 10,00. Other countries add .50 yearly additional charge. Remit by money order or draft on United States Bank. Single copy fifty cents. Subsciption limited to members of the profession and students of medicine.

ADDRESS CHANGES Notify us promptly of any change of address, mentioning both your old and new addresses. We cannot hold ourselves responsible if changes are not received as above. Complaints over three months old usually cannot be honored.

ADMINISTRATIVE AND EDITORIAL OFFICES: 1232-36 Central Avenue, Wilmette, Illinois.

EDITORIAL

Historical Priority in Medicine

by FREDERIC R. STEARNS, M.D.
Editor

In studying medical history, a very stimulating training field for the acquisition of criticism as to the highly praised 'progress', one is impressed by the fact how frequently the real pioneers are shadowed by the more extensive, yet less intensive accomplishments of successors.

In recent years, R. Wartenberg, in a number of papers and notes, was quoted for his special sphere of activitity, neurology, many cases in which historical priority had been given in the literature to authors or investigators who in fact were not the original explorers of the new experiences mentioned. It may be of some interest, in this respect, to expand Wartenberg's endeavors in establishing true historical priority. In the following we give just a few representative examples.

It is, of course, well known that Graves' disease which was described by Sir Robert Graves in 1835 had been already reported in 1825 by Thomas Parry and had been termed Parry's disease for quite some time. It may be less well known, probably, that Lutembacher's syndrome (mitral stenosis with auricular septal defect) was first observed by P. Ch. A. Louis in 1826 and was also recorded by Martineau in 1861; R. Lutembacher when he gave account of this syndrome in 1916 was already 90 years behind in historical sequence. Lobstein's disease (osteo-genesis imperfecta) has an almost similar historical course. J. Lobstein's publication appeared in 1834; yet, Elman had already in 1788 reported a case; and to complicate the historical picture even more, Vrolik in 1845 had also depicted the syndrome, and, consequently, in part of the medical literature it has been referred to as Vrolik's disease which, however, was identical with Lobstein's disease. Regards Pancoast's syndrome (superior pulmonary sulcus pressure syndrome), too, the priority question seems to be definitely solved; H. K. Pancoast's description, mainly on a roentgenological basis, was published in 1932, while the first report was made by E. S. Hare in 1838.

As to Kartagener's syndrome (transposition of viscera associated with bronchiectasis) Kartagener's paper of 1933 was preceded by that of Siewert in 1904. It is also interesting to note that peptic ulcer after severe burns, the so-called Curling ulcer, which was observed and published by Curling in 1842, had already been pointed to by Dupuytren in 1832. A particularly odd freak of misquotation of medical historical literature is connected with the discovery of the Ductus Botalli. It was not described by L. M. Botallus, at all, but by Carcano in 1599. What Botallus, himself, had demonstrated and termed as ductus Botalli, in 1564, was actually the post-natal patency of the foramen ovale. On the other hand, L. M. Botallus has the historical priority in pointing out allergic reactions in 1565 although the term allergy was coined by v. Pirquet in 1906. Alkaptonuria which recently has been rather frequently treated in medical literature is a dark coloration of the urine. The original paper is ascribed to Marcet

EDITORIAL

in 1823; but he has had two predecessors in the recording and observation of this discoloration: G. A. Scribonius in 1609 and Z. Lusitanius in 1649. J. Finsen is generally credited with the first account on epidemic pleurodynia (Bornholm's Disease) in a paper published in 1856; however, the very first presentation of this syndrome was given by G. Hannaeus (Hannes) in 1732.

It is somewhat astonishing that even in poliomyelitis historical priority problems could arise. Poliomyelitis was originally known as Heine-Medin Disease according to the clinical description of Jacob Heine in 1840 and the epidemiological delineation by Medin in 1890. Yet, the first presentation of the diseases goes back to Underwood in 1784.

Froehlich's disease (dystrophia adiposogenitalis) was not originally reported by Froehlich whose paper appeared in 1901, but by Babinski who published a case in 1900. Pierre Marie is believed to have first established acromegaly as a disease entity; yet, before him, the symptom-complex had been described by Sauccotte in 1772 and by Noel in 1779. Adie's syndrome (tonic pupil) was recounted by Adie in 1931; but long before his account two other authors, both in 1902, Saenger and Strasburger had published articles on the same observation. Thus, the note in the correspondence section of the J.A.M.A. of September 22, 1951 that C. Markus in England in 1906 was the first to describe this sign is obviously not correct.

W. W. Gull has been credited with the first paper on the syndrome of anorexia nervosa in 1868; yet, already in 1694, R. Morton had written on the same subject. G. V. Economo's name is closely linked with the original description of encepha litis lethargica in his famous articl in 1917. In 1916, however, Obregia Urechia and Carniol, had already in Rumania, depicted the syndrome V. Economo gave it the name. Wil son's disease (hepato-lenticula degeneration) was reported by S. A K. Wilson in 1912; but C. Westphall i 1833 had demonstrated the identica syndrome. Horner's syndrome (mi osis, ptosis of upper lid, enophtha mus, anhidrosis of skin of face, hy peremia of face) was not first pointe to by J. F. Horner in 1869 but b Hare in 1838.

Kümmell's disease (posttrauma tic necrosis) was first observed b Verneuil in 1892, two years befor Kümmell's p aper appeared (1894) As to Sprengel's deformation (con genital elevation of the scapula Sprengel was erroneously given pr ority with his article of 1891 as th deformity had been described al ready in 1883 by A. Willet and W J. Wallsham. The original accoun of the "milk leg", puerperal throm bophlebitis, has been attributed t Puzos in 1759; in fact, however, th first handed down report stems fro Mauriceau in 1668. Strümpell-Ma rie disease (rheumatoid spondylitis which was enlarged upon in two pa pers, by Strumpell in 1897 and b Marie in 1898, had been recognize and published already in 1893 b Bechterew. The discovery of the sta tus thymico-lymphaticus whic played for many years such an im portant role, particularly in Eur pean medicine, has been credited t Paltauf as its originator in 1890. Ye this condition had been observed an described already by F. Patter i 1641. Stevens-Johnson syndrom (eruptive fever) was not first poin ed to in the paper by A. M. Steven and F. C. Johnson in 1922; D.

Hebra in 1866 and E. Fuchs in 1876 had given account of this syndrome.

Quite striking is also the historical priority problem in Sturge-Weber Disease (encephalotrigeminal Angiomatosis). W. A. Sturge's report was published in 1879 and F. P. Weber's article appeared in 1922. Yet, a case had been recorded as early as 1860 by A. Schirmer. And while Weber is generally credited with the first radiological and anotomical diagnosis, S. Kalischer in 1897 already had published a case with evaluation of anatomical findings. Considering Tetralogy of Fallot, it is known that E. L. A. Fallot published his paper in 1888. While the first description of this congenital malformation is generally attributed to E. Sandford in 1777, the very first report, however, must be ascribed to Niels Stenson (Nicholaus Steno) under the date of 1671 and 1672. With respect to the Waterhouse-Friderichsen syndrome it is now recognized that the first demonstration of this disease stems from Voelcker in 1894-1895 while R. Waterhouse's paper appeared in 1911 and that of G. Friderichsen in 1918. A similar historical fate can be observed in Weber-Christian Disease (relapsing febrile nodular suppurative panniculitis). The earliest description was in an article of V. Pfeiffer in 1892; F. P. Weber reported on this disease in 1925 and H. A. Christian in 1928.

Examples like these could be easily multiplied. They are not only interesting from the viewpoint of the medical historian; they also prove that medical discovery is often rediscovery, and that medical progress is not always advance but recovery of hoary medical knowledge.

ORIGINAL ARTICLES

Therapy of Primary Atypical Pneumonia

By E. B. SCHOENBACH, M.D.

Department of Preventive Medicine, The Johns Hopkins University School of Medicine

Professor of Medicine, State University of New York, College of Medicine at New York

Director of Medical Services, The Maimonides Hospital of Brooklyn

"Primary atypical pneumonia is a respiratory disease which achieved clinical prominence following the introduction of successful antimicrobial therapy for lobar and other bacterial pneumonias. Because the course of primary atypical pneumonia was not influenced by the sulfonamide drugs or penicillin, it was attributed to a "viral" etiology. During World War II, the syndrome assumed real importance in that the incidence of this disease greatly exceeded all other types of pneumonitis among military and civil populations. The preliminary reports of Bowen (1935), Allen (1936), Longcope (1940), Kneeland (1940), and Dingle and Finland in 1942 were soon amplified by extensive studies on the clinical features and etiology.

No specific etiologic agent of primary atypical pneumonia has been isolated to date. The Commission on Acute Respiratory Disease at Fort Bragg demonstrated that pooled sputum from cases could transmit a similar disease to human volunteers even after it had been passed through bacteria retaining filters. However, the infectious agent was never concentrated or maintained in experimental animals. Eaton has isolated a virus from the sputum of patients which can be maintained through repeated passage in embryonated hens' eggs and which causes a pneumonitis in cotton rats. This virus has not been accepted as the etiologic agent of primary atypical pneumonia at present.

The pathology of the disease is still not clearly defined as the mortality rate is exceedingly low and most of the deaths have had complications. It is essentially a purulent bronchopneumonia from which various types of incidental organisms have been isolated at post-mortem examination. Although, clinically, there appears to be an atelectatic component, no bronchial plug or major involvement of the bronchi has been noted.

The onset of primary atypical pneumonia is often insidious and resembles a severe respiratory infection in which a persistent hacking, non-productive cough is present. Fever may be present at the onset, but often is not high until the second to third day of illness. It is associated with malaise, far out of proportion to the degree of illness evidenced by the patient, headache, and a rasping non-productive cough which often leads to hoarseness and aphonia.

Physical examination of the patient may show nothing more than diffuse redness of the mucous membranes of the throat and pharynx until almost the fourth to sixth day of illness when evidence of pneumonic involvement such as dullness and rales are elicited. Roentgen examination early in the disease may disclose pneumonic involvement. The pulse is frequently slow in proportion to the temperature. Rarely pleural reaction and effusion occur

in this syndrome. Unless secondary bacterial infection supervenes, the cough does not become productive but a thick mucoid sputum may be present.

The febrile period of the disease in a case of average severity is approximately 10 days. However, when large numbers of individuals are under close surveillance, as among the Armed Forces, many mild cases only detected by routine chest x-rays are encountered. Among the patients from civil populations admitted to a general hospital, the severity of illness is usually more marked and the febrile period more prolonged.

Complications are not common in this disease. Secondary bacterial invaders with purulent infection, phlebitis, sometimes associated with embolism, or erythema multiforme have been noted.

Except for evidence of pulmonary consolidation on roentgen examination, there are no specific laboratory procedures for identifying the disease. The patients usually have a real or relative leukopenia so that the white blood cell count usually does not exceed 10,000. The development of cold hemagglutinins for human group 0 erythrocytes and agglutinins for a strain of streptococcus MG has been repeatedly observed. However, these serologic reactions are of little aid during the acute disease as they do not become evident until the tenth to fourteenth day of illness and only 50 to 80 per cent of patients, in various studies, developed such agglutinins. Many other studies are usually performed to exclude diseases which resemble primary atypical pneumonia.

In summary, the diagnosis of primary atypical pneumonia is based upon the following criteria:

1. The onset is gradual with nonproductive cough, fever, malaise, and occasionally substernal pain. T absence of initial chill, bloody sputum and abrupt onset aid in the differentiation from lobar pneumonia.

2. Physical examination often does not disclose pneumonic involvement commensurate with that noted on roentgen examination.

3. Laboratory examinations show a low or normal leukocytic count. Pneumococcic or other organisms commonly associated with pneumonia are not present in the sputum, throat, or nasopharyngeal cultures.

4. Serologic studies on serial serum specimens do not reveal the development of antibodies for the recognized viral or rickettsial agents.

5. The appearance of cold hemagglutinins for human group 0 cells or agglutinins for the streptococcus MG during the course of the disease or convalescence in a high proportion of the cases in an outbreak.

6. Treatment with sulfonamides or penicillin is not associated with clinical or objective improvement in the uncomplicated case.

In the individual patient, it is difficult to differentiate primary atypical pneumonia from many other types of pneumonitis without extensive study. This is not a problem to the physician who will usually be confronted by many cases when the disease strikes a community but great care must be exercised not to label any patient who has not responded to antimicrobial therapy as primary atypical pneumonia. The diseases which have been confused with primary atypical pneumonia are: infectious mononucleosis, influenza, lymphocytic choriomeningitis, ornithosis, Q fever, typhoid fever, brucellosis, tularemia, tuberculosis,

and pulmonary neoplasm. It is difficult to differentiate these diseases even in retrospect without the aid of specific serologic or other laboratory aids. The index of suspicion should be great especially if the patient is seen at a time when little respiratory disease is occurring among the population in that area. This is especially true now that some of the newer antibiotics are available which will influence the course of some of these diseases. Treatment may be insufficient and apparent relapse may be shown to be due to unsuspected brucella or typhoid bacillus infection.

The treatment of primary atypical pneumonia consists of general supportive and nursing care supplemented by specific chemotherapy. It has been clearly shown that aureomycin, terramycin, and chloramphenicol will definitely shorten the duration of fever and illness. Although the major experience has been with aureomycin, preliminary reports indicate that chloramphenicol and terramycin are effective. Oral administration is effective.

The dosage of aureomycin recommended is approximately 40 mg/kg of body weight per day (2.0 grams for a 50 kg patient) divided into four to six doses. The dosage may be increased for severely ill patients to 50 or 60 mg/kg per day and reduced to 20 or 30 mg/kg in mild cases. This initial daily dosage is continued until the patient becomes afebrile and then may be halved until the aureomycin is discontinued. The average duration of treatment among a series of hospitalized patients was five days and the median amount of aureomycin employed was 7.0 grams. The dosage of terramycin is similar to aureomycin. When chloramphenicol is employed an initial loading dose of 20 mg/kg of body weight should be administered (1.0 grams for the average adult) at hourly intervals for three doses and thence continued at intervals of six hours until the patient becomes afebrile. The dosage may then be halved for several days until it is discontinued. Parenteral antibiotic therapy is not required in primary atypical pneumonia.

The results of therapy have been most gratifying. One may cite a study in which the results among patients with primary atypical pneumonia who were treated with penicillin and/or sulfonamides were compared with the results among a similar group who received aureomycin. The median duration of illness preceeding hospitalization and aureomycin therapy was approximately 5 days for both groups. The patients treated with penicillin remained febrile for 5 to 6.5 days while those receiving aureomycin became afebrile within 1.5 to 2.0 days. Clinical improvement appeared to parallel the febrile defervescence and no progression of pulmonary involvement was observed after initiation of therapy. The hacking cough, however, may persist for a long time after other clinical manifestations of illness have disappeared. The rate of clearing, as indicated by roentgenograms of the chest, may be quite slow and the effect of antibiotic therapy can not be assessed.

Complications of antibiotic therapy have been minimal except for anorexia, nausea, emesis, and diarrhea. These may be regarded as annoying rather than serious. Stomatitis which may represent a nutritional deficiency or secondary overgrowth with Candida has been uncommon among patients treated for the period required.

It has been our experience that, since the introduction of aureomycin, chloramphenicol, and terramycin as therapeutic agents, an increased number of patients have been referred to the hospital with the diagnosis of primary atypical pneumonia who have been shown to have tuberculosis or neoplasm. Attention, therefore, is again directed to careful evaluation of patients with atypical pneumonitis who do not promptly respond, or in whom, despite febrile lysis, evidence of extension occurs after treatment with the newer "broad spectrum" antibiotics.

References

1. Schoenbach, E. B., and Bryer, M.S.: *Treatment of Primary Atypical Non-bacterial Pneumonia with Aureomycin*, J.A.M.A. *139:* 275-280, 1949

2. Collins, H. S., Wells, E. B., Gocke, T. M., and Finland, M.: *Treatment of Primary Atypical Pneumonia with Aureomycin* Am. J. Med. *8:* 4-20, 1950

3. Schoenbach, E. B., Sweed, A., Tepper, B., and Bryer, M. S.: *An Evaluation of Aureomycin Therapy in Primary Atypical Pneumonia* N.E.J. Med. *243:* 799-805, 1950.

4. Kneeland, Y., Jr., and Melcher, G. W: *Terramycin in the Treatment of Primary Atypical Pneumonia* Ann. N. Y Acad. Sci. *53:* 437-439, 1950

Celiac Syndrome

By ROBERT B. TUDOR, M.D.

At the present time the celiac syndrome is considered by most observers to be a large heterogeneous group of conditions each of which has chronic or recurrent diarrhea as the main symptom. The term steatorrhea is not a good description of the abnormal stools, for in many cases an excess of fat is not present.

The diarrhea may begin at any age from birth to the age of six years. We do not ordinarily see this condition begin much after the age of three years, however.

As a large number of unrelated conditions may produce chronic diarrhea in the child, I will discuss only the most common.

Chronic or recurrent stooling, or diarrhea beginning shortly after birth, up to the first six months of life should suggest one of the following causes:

1. An anomaly of the urinary tract, such as hydronephrosis, or hydroureter, usually associated with urinary tract infection.

2. Malrotation of the gut.

3. Fibrocystic disease, also usually associated with a poor weight gain and frequent bouts of respiratory infection.

4. Celiac disease, most cases of which begin after the first six months of life.

After the first six months of life, chronic diarrhea should suggest one of the following:

1. Infection, usually in the tonsils, adenoids, ears or sinuses.

2. Celiac disease, which has been characterized by Andersen as a chronic or recurrent diarrhea occuring usually after the first six months

of life without demonstrable bacteriologic, anatomic, or, I will add, enzyme basis.

3. Fibrocystic disease, which occasionally begins after the age of six months.

4. Following surgery to the gut, such as removal of a portion of the small intestine due to bowel obstruction or peritonitis. I have seen this several times.

While this list of conditions usually associated with recurrent diarrhea includes the usual causes, it is by no means complete. A few rarer causes would include hypothyroidism, allergy and chronic enteric infection with Ascaris, Giardia or Salmonella.

Diagnosis

If one has a plan of attack when faced with a child with chronic diarrhea, this whole subject is greatly simplified.

A physical examination is the first step. This should help in ruling in or out a respiratory infection. Laboratory examination in the office should then include a white blood count, a differential, nose and throat cultures, sinus x-rays (when indicated) several urine examinations and a stool culture. The finding of inflamed tonsils or ears, an elevated temperature, a streptococcus in the nose and throat culture, an elevated white count, pus in the urine, or an organism in the stool culture should determine whether or not infection is present.

The next step in the diagnosis should be a careful examination of the child's duodenal juice for amylase, lipase and trypsin.

Intubation of the child's duodenum is not difficult once the technique has been mastered. The tube should be passed under fluoroscopic contol. I use a twelve, fourteen, or sixteen French nasal suction tube, fairly new if possible, which has holes extending not more than two or three inches up from the tip. This tube should be passed preferably in the morning after the patient has fasted all night. Sedation of the child during the procedure is not necessary, and may be harmful, as it decreases the output of enzymes from the pancreas. If the child is mummied before the tube is passed and kept in this state until all the necessary fluid is obtained, the procedure usually goes without a hitch. Many times the tip of the tube can be passed immediately into the duodenum, whence it quickly is pulled along by peristaltic waves and the pancreatic fluid obtained, within fifteen to twenty minutes. If the tube will not go immediately into the duodenum, its tip should be left approximately at the pylorus and the child turned on his right side. Gentle suction on the tube may be necessary to get the fluid to run easily, but too frequent or too strong suction should not be done, as it usually sucks some intestinal mucosa up to the intestinal end of the tube and consequently no fluid will then flow through the tube. The fluid should be collected in a test tube immersed in a beaker filled with ice and only the alkaline juice saved (i.e. only juice which will turn PH paper from orange to green, blue or black).

Any good laboratory can examine the duodenal juice for amylase, lipase and trypsin.

An intravenous urogram or planogram is next in order to determine whether or not one is dealing with an anomaly or other defect of the kidneys, ureters or bladder.

Last of all, one should do a barium enema to determine whether the patient has any anomaly of the gut. This of course would not be necessary in those children who have had

a portion of the gut excized for some acute surgical condition.

Almost every case of chronic or recurrent diarrhea in infancy and childhood can be diagnosed in this way.

Therapy

The treatment of infections of the respiratory tract, urinary tract and gut is obvious so will not be discussed. Suffice it to say that treatment should be accurate, adequate (in dosage) and last three to six weeks in most children, only then will the diarrhea cease.

In cases of anomalies of the gut, kidneys, ureters or bladder amenable to surgery, this should be carried out.

The largest group of these children will fall into the group where there is some proved or suggestive deficiency of one of the pancreatic enzymes. Treatment of this group even in many cases of pancreatic fibrosis, if done carefully and adequately is most satisfying to patient, family and doctor.

In fibrocystic disease, one usually finds greatly decreased or absent trypsin in the pancreatic secretions. Treatment is as follows:

1.) A full diet, high in protein containing foods.

2.) At the present time sulfadiazine given in dosage of one-half gram a day or aureomycine in a dosage of 50 to 100 mgs. a day has given the best results in preventing the respiratory infections these children fall heir to. In my own hands, sulfadiazine has given me the best results.

3.) Adequate and early treatment of each flare up in the respiratory picture.

4.) Pancreatic granules given in dosage of ten to fifteen grams a day. If the child is nauseated following ingestion of pancreatic granules, they may be discontinued.

5.) Adequate vitamin intake. This should include vitamin C, vitamins A and D, and vitamin B complex, all given orally. It has been suggested that about double the average dose of vitamins should be offered these children.

In celiac disease, in which all enzyme determinations are usually normal, but in which one may find an excess of fat or starch or both in the stools, there is a controversy at the present time as to etiology. Andersen and the Haas's feel that this is an amylase deficiency disease. Most others, and I would have to concur with this, feel that a definite etiology has not yet been found.

The accepted plan of treatment for this large group of children, with celiac disease, whether one holds to the current concepts of its causation or to Andersen's newer findings is as follows:

1.) A diet high in protein, supplied as meat, cheese, gelatine, egg, fish, fowl and protein milk or calcium caseinate milk.

2.) The amount of fat given should be limited at first to that present in meat, small amounts of butter and in milk. As the child responds to therapy, fat in other foods is gradually added.

3.) Carbohydrate is given in the form of ripe bananas or banana powder and of course in the protein or calcium caseinate milk. As the diarrhea subsides other fruits are gradually added, and finally vegetalbles are offered. Canned fruits which have added sugar and any food which does not have

naturally occuring sugar is excluded from the diet at first.

4.) Cereal, bread and potatoes are not tolerated well.

5.) In 1942 May, et al found that by giving alternate injections of crude liver extract and parenteral vitamin B complex every other day for about three weeks, and then continuing with oral vitamin B complex, a definite improvement was noted in three to six weeks. I have used this method of treatment many times with success. Vitamins A, D and C should also be given by mouth in about twice the normal amounts.

Summary

The diagnosis and treatment of infants and children with chronic or recurrent diarrhea is facilitated by a careful physical examination, a few essential office laboratory tests, duodenal intubation with examination of the duodenal juice for trypsin, amylase and lipase, an intravenous urogram and a barium enema.

Good results follow treatment in almost all cases.

Bibliography

1. Andersen, D. H.: *Celiac Syndrome* J. of Peds 30:564, 1947

2. May, C. D., McCreary, J. F. and Blackfon, K. D.: *Notes Concerning Cause and Treatment of Celiac Disease;* J. Ped 21:289, 1942.

3. Haas, S. V. and Haas, M. D. *Diagnosis and Treatment of Celiac Disease* Post grad Med.; 7:239, 1950.

4. Wolman, I. J.; *The Intraduodenal Secretions in Childhood;* Am. J. of Med S. 209, 788; 1945.

5. Tudor, R. B.; *The Celiac Syndrome* Journal Lancet, 142, May 1946.

6. Farber, Sidney; *Pancreatic Insufficiency and the Celiac Syndrome;* New Eng. J. of Med. 229-653, 1943.

"Alkaptonuria"

By CARL L. MAUSER, M.D.

Oakland, California

Although alkaptonuria was recognized many years ago, perhaps as early as the sixteenth century, it is still considered a very infrequent disease.[1]

Because of the confusion that may arise between diabetes mellitus and alkaptonuria, it is important to recognize this unusual error in metabolism. Garrod[2] states that Luistanus[3] first reported a case of this unusual condition in 1649. The patient was a male who first passed black urine at the age of fourteen. He lived to a normal age and raised a large family but continued to pass urine as black as ink all his life in spite of a great deal of symptomatic and unusual intensive therapy. The clinical manifestations of alkaptonuria were first described by Marcet[4] in 1823 and the disease was apparently first desribed by the name, "Alkaptonuria", by Boedeker[5] in 1859. The nature of the reducing material in the urine was first recognized by Marshall[6].

Alkaptonuria is an error in protein metabolism resulting in the excretion of homogentisic acid in the urine. The urine may be dark when first passed or it may turn dark

on standing or after the addition of an alkali. The two amino acids that have been incriminated as the source of abnormal metabolism are tyrosine and phenylalanine. These two amino acids are the precausers of homogentisic acids, which is the result of the breakdown of tyrosine and phenylalanine. The inability of the body to split open the benzine ring which is contained in these acids causes the cessation of the breakdown and at this point, homogentisic acid is excreted in the urine. It is thought that, genetically, albinism and alkaptonuria are similar, since both are controlled by mendelian recessive genes. Inbreeding is thought to have some affect in the precipitation of this condition in individuals. Eisenberg[7] states that tyrosine is the chief chromogen, or pigment-supplying substance, in the animal organism. In albinism, the mechanism for converting tyrosine to pigment is lacking. He believes that in alkaptonuria, the mechanism for breaking down tyrosine futher than homogentisic acid is lacking.

Patients with alkaptonuria usually have no clinical manifestations unless there is pigmentation of the cartilages, called "Ochronosis". The condition is usually considered to completely benign. The urine, on standing, becomes alkaline and gradually turns brown to black without sedation of the homogentisic acids. The recognition of the disease is usually done by various tests:

1. The urine, on standing, becomes alkaline and gradually turns brown to black without sedation of the homogentisic acids.

2. The addition of alkaline produces a similar affect. The homogentisic acid itself reduces alkaline solutions, such as Benedict's or Fehling's solution and may thus be mistaken for glycosuria.

3. Alkaline bismuth solutions are not reduced.

4. Silver lactate solution (Nylander's reagent) is reduced in cold.

5. When 10% sodium hydroxide solution is added to a urine containing a homogentisic acid is black precipitated form.

6. Silver nitrate solution is reduced in cold.

7. The addition of 1 - 10% solution of ferrichloride to 5 ccs. urine produces a transitory bluish or greenish coloration.

Other tests which may be of benefit are:

(a) Homogentisic acid does not ferment yeast

(b) Homogentisic acid does not rotate polarized gluocse.

(c) The addition of Mellin's reagent produces a yello precipitate.

The simple test for the presence of homogentisic acid depends upon the relationship of hydroquinone. A drop of urine, which has been made alkaline, when placed on sensitized photographic paper, immediately becomes black. This color change does not occur with normal urine.

Diagnosis

The diagnosis of alkaptonuria is not significant clincially, and persons having the disease, in most instances, appear to enjoy good health and seem normal in all other respects. Occasionally there are associated symptoms as stated above, or ochronosis. There are three symptoms which are most frequently associated and recognized in making a diagnosis of alkaptonuria:

1. The dark color of the urine perse, or on standing.

2. Pigmentation of the sclera and ears.

3. Arthritis.

Ochronosis is a condition that occurs quite frequently. It is present in about half of the patients with alkaptonuria after middle age and is much more prone to occur in people after this period of life. Ochronosis of the tendons, cartilages, ligaments and intima of the lage vessels. The general description of the pigment is usually that of a grey or bluish-black which appears yellow under the microscope, thus giving the name of the symptom, "Ochronosis". So far as sex incidence is concerned, it is about equal in both, although some authors state that they believe the condition to be more prevalent in men. It has been described in the early twenties and as late as in the eighty-fifth year of life. The average age is about fifty years. The pigmentation lies in the fibrous cartilagenous structures, the sclera, the center external cartilages, the tendons and the skin. The sclera frequently take on a profuse grey color. There is often associated a semi-lunar or "V"-shaped patch of pigmentation in both sclera. The pigmentation may acquire the size of a bean and is situated midway between the margins of the cornea on the outer or inner canthus. The color may vary from deep brown to black. The characteristic location for pigmentation of the cartilages and fibrous tissue is the ear. The skin of the face may be involved and may also be described as a coffee colored, diffuse coloration. At times there is a uniform yellow-brown coloration with intensification over the malar areas of the face. Hartzberg and Soderbergh[9] both have described an articullar involvement in alkaptonuria. The arthritic changes seem to be of a hypertrophic nature and may affect any of the joints, particularly the spine. Pomeranz, Friedman and Tunick[10] felt that the posture of these patients wa compatible with Paget's disease The bony changes may be indistin guishable from those of osteomala cia except for the absence of pig ment in the latter disease.

Alkaptonuria or ochronosis usual ly run a chronic course over man years and generally terminate i some affection of the arterio system Blackish pigmentation of the valv of the heart and the intima of th aorta and iliac arteries has been de scribed several times by Tick.[11] The case of Eisenberg[7] mentions hepati lesions.

Prognosis:

Prognosis is usually excellent fo life expectancy and treatment is pro phylactic or symptomatic. Avoidin the prolonged use of phenol prepara tions is thought to be of some valu in preventing the changes that occu due to the abnormal metabolism o the amino acids mentioned above It may be that alkaptonuria, bein a congenital or familial disease could be avoided by preventing in termarriage between affected fami lies.

Conclusion:

1. Alkaptonuria is an unusual con dition frequently associated wit ochronosis and arthritis.

2. Alkaptonuria is asymptomati so far as the patient is concerne apart from arthritis.

3. The symptomatology with whic one can recognize alkaptonuria i the changes that occur in the urine either spontaneously, by oxidatio or by alkanization, or one of the test mentioned above. Ochronosis an arthritis are of benefit.

4. The family history of the pati ent may be of some help in deter mining whether the condition is fam ilial or hereditary.

5. The condition has no particula

value except from the academic standpoint. It may be confused with diabetes mellitus and when this occurs it is important to have glucose determinations run on the urine and blood.

6. These people have normal life spans and usually die of some unrelated pathological condition.

Bibliography

1. Mauser, Carl L: J.A.M.A., 149:9, June 30, 1951, p. 185.
2. Garrod, A. E: *Inborn Errors of Metabolism*, ed. 2, London, H. Frowde & Hodder & Stoughton, 1923.
3. Lusitanus: *Praxis Medica Admiranda*, book 3, chap. 134, 1649.
4. Marcet, A: Tr. Med-Chir. Soc. Edinburgh, 12: 37-45, 1822-1823.
5. Boedeker: *Ueber das Alcapton*, Ztschr. f. rat. Med. 7:130, 1859; Ann. Chem. d.u. Pharm. 117: 98, 1861.
6. Marshall, J: M. News 50; 35, 1887.
7. Eisenberg, H: Archives of Int. Med. July 1950., p. 80.
8. Hertzberg, J: *On Osteoarthrosis Alkaptonuria (Ochronotica)* with Description of Case, Acta radiol. 26:484, 1945.
9. Soderbergh G: Nord. Med. Ark., 1915, vol. 48, no. 4, pt. 2.
10. Pomeranz, M.M.; Friedman, L. J.: & Tunick, I. S.; *Roentgen Findings in Alkaptonuria Ochronosis, Radiology*, 37: 295 (Sept.) 1941.
11. Tick, A: As reported by Eisenberg, H; Archives of Int. Med. July 1940., p. 80.

The Care of Varicose Veins by the General Practitioner

By S. M. RECKLER, M.D.
Denver, Colorado

Varicose veins have been treated since time immemorial. Their existence is antedated only by man's elevation of himself to his hind legs. They are uncommon in youth and develop as the middle decades are approached.

Heredity is the greatest single etiological factor and it is statistically true that four out of five patients give a direct familial history. Inherited weakness of the valvular and wall structure of the venous sytem is the basis upon which varicosities develop. Superimposed upon this weakness are assumption of the upright position, pregnancy, occupational stress, systemic disease with overloading of the venous system and smoking with its attendant vasospasm. As a result of these factors, varicose veins appear; their valves become incompetent and dilatation venostasis result. If unchecked at this stage, chronic eczema, anoxia, migrating superficial thrombophlebitis, fibrosis, chronic lymphedema and ulcer follow.

In order to logically treat varicose veins, it is paramount that the anatomy and pathological physiology be fundamentally understood. The physical examination should be conducted intelligently and knowingly. Treatment will then be found to be easy and gratifying to both the patient and the doctor.

The venous systems of the lower extremities are three in number—

saphenous, communicating and femoral. The saphenous system is comprised essentially of the long and short saphenous veins. The long saphenous vein originates along the medial aspect of the dorsum of the foot. It travels along the medial aspect of the ankle, leg and thigh to reach the groin where it joins the femoral vein at the fossa ovalis. The short saphenous vein originates on the lateral aspect of the foot and travels along the lateral and posterior aspect of the leg and joins the popliteal vein in about sixty per cent of the cases; in thirty per cent, it enters the deep circulation elsewhere and in ten per cent, it joins the long saphenous vein. The communicating veins join the saphenous venous system to the femoral venous system and are about five in number above the knee and twenty in number below the knee. The femoral venous system is well supported by its subcutaneous and muscular surroundings and rarely becomes varicose or incompetent except as a consequence of femoral thrombophlebitis. Of clinical importance are the constant superficial inferior epigastric vein, the superficial external pudendal vein, the superficial circumflex iliac vein and the less constant lateral and medial femoral cutaneous veins, all five of which empty into the greater saphenous vein just distal to the sapheno-femoral venous junction.

Let us now consider the basic pathological physiology that has been alluded to briefly already. A vein wall consists of three layers, an intima, media and adventitia. The intima is a single layer of endothelial cells; the media is fibro-elastic tissue and smooth muscle tisue and the adventitia is fibrous tissue. Contained within the veins are valves which, in health, prevent backflow. Veins carry blood from venous capillaries back to the heart and secondarily serve as reservoir spaces for storage of blood. The venous blood of the lower extremities is propogated by venous capillary pressure and surrounding leg muscle contracture.

So long as the valves remain competent, regurgitation cannot occur and varicosities do not occur. However, the constant stress and strain on the inherently defective valvular structure takes its toll as middle age approaches and the other factors previously discussed exert their contributory harmfulness. The retrograde hydrostatic pressure of the involved vein becomes ever greater. Dilatation begins and progresses as the wall loses its power to hypertrophy as a compensatory mechanism. It becomes thin and fibrotic. The superficial skin and subcutaneous tissue become filled, and later edematous with venous static blood. Lack of oxygen to these structures manifests itself with progressive development of brawniness, discoloration, fibrosis and, finally, ulcer formation.

The symptoms associated with varicose veins are quite obvious. They are the result of the disturbed physiology and vary with the extent of this disturbance. There may be pain below the knee levels, particularly upon prolonged standing. As a generalization, pain above the level of the knees is not due to varicose veins. This leg pain is usually relieved by rest and elevation. Heaviness of the legs, edema and swelling are present in severe cases. Where ulceration has occurred, secondary fungus infection may be expected with severe anoxemia. The skin may be fibrotic, thick, tense and discolored.

Proper physical examination is within the power of every physician.

be he a general practitioner without hospital facilities or a large city specialist with every hospital facility at his slightest request. Intelligent application of a few simple tests reveals the status quo of the patient and the treatment indicated. Every patient needs a complete history taken as well as investigation of his general condition. The history of femoral thrombophlebitis in the past and recurrent ulceration necessitate investigation of the deep circulation with particular care. A Kahn test and a urinalysis are a must in diagnosis.

If the femoral circulation is inadequate, any major attack upon the saphenous system will be catastrophic. For indeed, many so-called varicosities of the saphenous systems are in reality compensatory hypertrophy of the saphenous systems as the result of incompetent and inadequate femoral venous systems.

How can we know that a deep system is adequate and competent? Short of venography of the femoral system, our approach to this problem is a negative and yet satisfactory one. We eliminate, temporarily, the saphenous system and see if the deep system can carry out the job of the lower extremity venous return. It is called Perthe's test. The leg is elevated, the blood is massaged out of the leg, snug bandages are applied from the toes to the groin and the patient allowed to walk for fifteen to thirty minutes. If the femoral vein return is good, no pain will be elicited. Conversely, if crampy pain occurs in calf or general discomfort in the leg in general, resulting from venous pooling in the leg, then it is assured that the femoral circulation is inadequate and that the test is positive. Similarly, the test can be carried out using multiple tourniquets at various levels of the lower extremity.

Examination of the saphenous system is now in order. Many tests have been described and names applied to them. While memorizing of names may be well for students and text books, the author's approach is based upon a combination of tests and aims at an understanding of where the incompetency or incompetencies exist. If a leg is elevated, the saphenous venous blood massaged out of the leg and a high rubber tourniquet applied and the patient then be allowed to stand, one of several things will be noted. First, if the tourniquet is released and the venous system fills slowly, thirty to fifty seconds, from below upward, then the sapheno-femoral venous junction is adequate. Secondly, if the saphenous system fills rapidly from above downward, then the saphenous femoral junction is inadequate. Thirdly, if the vein fills rapidly from below upward, upon release of the tourniquet, but not from above downward, then the communications are inadequate. Fourthly, if the filling of the vein, upon release of the tourniquet, occurs rapidly from above downward and below upward simultaneously, then we are dealing with incompetency of communicating vessels in addition to the inadequacy of the sapheno-femoral junction. By varying the positions of multiple tourniquets, levels will be found at which imcompetent communicating vessels exist as evidenced by rapid local filling between tourniquets.

The reader is referred to standard texts for classical description of Schwartz's, Trendelenburg's and Mahorner tests for incompetency. Their restatement by me would be superfluous. The essential facts to

be determined by examination have now been explained.

If one is satisfied that the femoral circulation is adequate, then saphenous treatment can be undertaken with safety. The fundamental question to be considered is this, "How much treatment can a general practitioner undertake with limited facilities?" My answer is direct and simple, "As much as he feels qualified to do with whatever facilities are available." Many large vascular clinics perform their saphenous surgery in the out-patient department and send their patients home post-surgery. I feel that the answer lies with each man's own conscience. Examination and treatment are relatively simple if based on knowledge and experience. Mistaken ligation of femoral arteries and femoral veins are frequently reported. One must remember that an error of this magnitude results in tragedy. Visits to vascular clinics, post-graduate courses, stated medical society visiting clinics are available for refreshing one's knowledge of the subject.

I shall now describe specific treatment of varicose veins, as a guide, to those who would feel qualified and equipped to undertake such treatment. As a generalization, local infiltration anaesthesia with 1% or 2% novocain solution will suffice for all surgery, with the possible exception of saphenous stripping. Here general induction or spinal anaesthesia is indicated because of the pain attendant to its performance.

The simplest type of treatment are minimal varicosities with competent saphenous trunks. Patients with such pathology usually present themselves for cosmetic reasons. These can be treated by injection of sclerosing solutions. There are a number of acceptable solutions some of which are less irritating to extravenous tissues, if accidentally deposited out of the veins, than others. My own preference if for 5% solution of Sodium Psylliate, under the trade name of Sylnasol, and 3% solution of Sodium Tetradecyl Sulfate, under the trade name of Sodium Sotradecol. Other solutions include 5% solution of Sodium Morrhuate and a mixture of 25% dextrose and 17% sodium chloride. There are a number of others. A minute subcutaneous preliminary skin test is always indicted before injection of a vein. The purpose of a sclerosing injection is not to coagulate the blood alone but, much more importantly, to so irritate the endothelial lining of the vessel that the walls will become adherent and obliteration of the lumen will occur. My own preference is to apply a tourniquet above the site to be injected and, with leg in a dependent position, to introduce a No. 25 needle into the vein, inject a maximum of 1 cc of solution at any one time, release the tourniquet, wrap an alcohol sponge firmly over the site and tape in place, leaving same for four hours.

If the sapheno-femoral junction is incompetent, saphenous ligation at that level must be done, together with the ligation of the corallary branches mentioned in the anatomic description above. Through an oblique incision paralleling the inguinal ligament, with its mid-point 1 cm. inferior and 1 cm. medial to the maximal impulse of the femoral artery as it emerges through the femoral canal, the sapheno-femoral junction is easily approached. Type of suture material varies with the individual, preference of the operator and the weight with the size of the involved vessels. My own preference is for catgut, varying from 000 plain to No. 1 plain, with transfixion of the larger vessels. For skin

closure, my preference is No. 00 silk. Wherever incompetent communicating vessels are demonstrated, ligations of the communicator as well as the saphenous vein are likewise carried out. A very constant site of incompetency is just above the knee and ligation at this level is referred to as a low saphenous ligation. All ligations are followed by sclerosing injections if any segments of vessels remain patent. Multiple ligation therapy is carried out when a number of incompetent segments are present, each fed by an incompetent communicating vessel.

It is my personal feeling that strippings are hospital procedures and require general anaesthesia. For those who may be so equipped, may I say that these are most easily accomplished by use of Babcock type of intra-luminary strippers which are passed from below upward, starting at the level of the medial malleolus in case of the greater saphenous and passed to the groin if possible. The lesser saphenous is stripped from the postero-lateral part of the leg to level of popliteal space. Thrombotic, tortuous and adherent veins preclude stripping and excision or forcible evulsion may be necessary. Elastic wrappings of the legs must be carried out post-operatively, both to minimize post-operative hematomata and to limit transitory swelling. Complications of varicose veins usually require hospitalization if very severe. Pulmonary and cerebral emboli are rare, fortunately, and are treated as any sort of embolic phenomenon. Rupture of a varix is best treated by pressure and elevation. If need be, ligation of the involved vessel may be required. The commonest complication is ulcer formation and its cure is dependent upon the control of the basic condition. Skin grafting may also be necessary in severest cases. Temporary relief from the discomfort and disability attendant to varicose ulcer treatment may be had from Unna Boot application, pressure dressings, bed rest and elevation of the affected leg. Eczema associated with varicose veins likewise requires elimination of the varicose condition and may in addition require topical therapy as the eczema may become chronic and extend far beyond the confines of the varicose vein condition.

Finally, I should like to mention that, because of the tendency of the varicose vein patient to develop new veins of the same type that have just been treated, we must continue to keep these patients under observation. We must attack these new vessels early with injection and obliterate them before associated incompetencies can develop to complicate their treatment. If the type of work one does requires protracted standing, the use of elastic bandages or stockings is indicated. We are obliged to treat a continuing disease, for we are at a loss to affect any change, therapeutically, in its primary nature.

The Mechanism of the Menopausal Syndrome

By ERNEST F. HOCK, M.D.

From the Department of Urology, Charles S. Wilson Memorial Hospital, Johnson City, New York

Improvement of menopausal symptoms following the administration of estrogenic substances has led to the conclusion that a hormonal imbalance may be the direct cause of these symptoms. No doubt, many postmenopausal changes can be explained by a disturbance of the hormonal equilibrium; however, all attempts at discovering the mechanism of such symptoms as flushes, vertigo, nervousness, abnormal fatigue, aches in various parts of the body and "rheumatism" have been unsuccessful. In spite of extensive research done in this field, no correlation could be established between the severity of these symptoms and the amount of estrogenic and gonadotropic hormones in the blood and urine. Other facts that cannot be explained on a purely hormonal basis are the following:

1. Not every woman in her menopause experiences menopausal symptoms. According to Barrett, 15.8% of a thousand women in their menopause were completely free of menopausal symptoms.

2. Some women having normal menstrual cycles and whose vaginal secretions and epithelium indicate estrogenic activity, complain of typical menopausal symptoms.

3. Hysterectomy alone with retention of both ovaries may cause severe menopausal symptoms.

4. Artificial menopause in young women is not always accompanied by menopausal symptoms.

5. Not every woman suffering from menopausal symptoms is relieved by estrogenic hormone.

A possible explanation of the mechanism of menopausal symptoms was accidentally found during a study of the symptoms caused by prostatic disease. Thirty patients with various types of prostatic pathology were carefully questioned about the details of their symptoms. Most of these patients suffered from prostatitis or from early enlargement of the prostate. Chief complaints were backache, disturbances of micturition, vague constitutional and genital symptoms, rheumatism and urethral discharge in that order. Simple therapeutic procedures such as prostatic massage or passing a sound through the urethra into the bladder were used as tests in order to distinguish between symptoms of prostatic and nonprostatic origin. If a patient felt improvement of a particular symptom after these tests, it was concluded that the symptom had been caused by the prostate. Aggravation of the symptom following the test also pointed to the prostate as the origin of the trouble. If the patient felt no change, it was assumed that the prostate was not responsible for the symptom

A detailed analysis of the symptoms is given in Table I.

The prompt response of these symptoms to therapeutic procedures on the prostate suggested a reflex mechanism, the prostate being the focus of irritation. Since, in the female, the urethra is the homologue

TABLE I

Analysis of Symptoms in 30 Patients with Prostatic Pathology

Symptoms	Number of Patients
Disturbances of urination	
Frequency	12
Nocturia	12
Burning	16
Difficulty in starting voiding	11
Dribbling after voiding	18
Tickling while voiding	1
Stress incontinence	2
Aches in various parts of the body	
Backache, sacroiliac	16
Backache, lumbar	17
Ache in scapular regions	9
Pain in perineum	6
Hypogastric pain and discomfort	8
Pain:	
Inguinal	12
Thigh	13
Knee	9
Legs	7
Foot	2
Upper extremities	6
Paresthesias:	
Upper extremities	4
Lower extremities	8
Night cramps in lower extremities	2
Constitutional symptoms	
Headache	12
Fatigue	26
Nervousness	21
Hot flushes	15
Excessive perspiration	14
Dizziness	9
Disturbances of genital functions	15

of part of the prostate, the conclusion that similar symptoms in women could have their origin in the urethra did not appear unreasonable. In practice, it was found that the effect of passing sounds into the female bladder was identical with the result of prostatic massages or passing urethral sounds in men. If now the table listing the symptoms of male patients with prostatic disorders is reviewed, it will be found that these symptoms are practically identical with those of the menopausal syndrome. This similarity suggests that menopausal symptoms may be the result of an irritative nerve lesion in the female urethra. The fact that the characteristic symptoms usually appear at the time of the menopause indicates that the irritative nerve lesion may be the result of, or aggravated by, estrogen deficiency. It is known that deficiency of estrogens is followed by degenerative changes in the urethra in a similar way as it produces senile vaginitis and other degenerative changes of the genital tract. It is possible that degeneration of urethral tissues alone is able to produce nerve irritation, or these urethral changes may predispose to a secondary infection. Treatment with estrogens then would relieve menopausal symptoms indirectly by first correcting the changes in the urethra.

Figure I is a diagrammatic presentation of our theory of the mechanism of the menopausal syndrome.

(Figure 1 appears on next page)

Comment

The author does not wish to create the impression that he tries to explain all features of the menopausal syndrome on the basis of a urethral causalgia. There is no doubt but that hormonal factors influencing the whole organism are also involved. It is possible that a hormonal imbalance may increase the reflex irritability of the nervous sytem, e.g. by hypersecretion of thyroid hormone, and thus facilitate a causalgic process. The main point stressed here is that a causalgia is a factor in

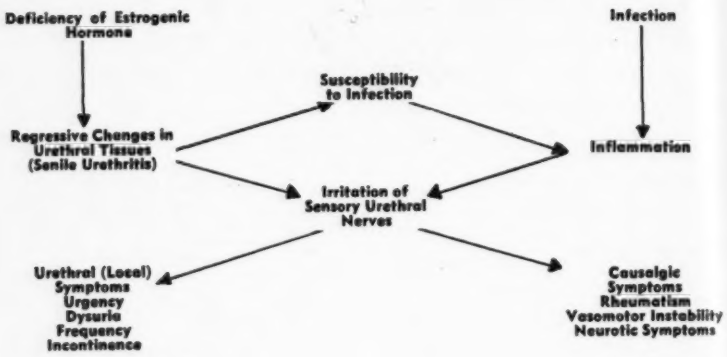

Fig. 1. Diagrammatic presentation of theoretic mechanism of menopausal syndrome.

the production of menopausal symptoms. It is likely that reflexes from other organs which are connected with important nerve plexuses can cause similar symptoms; however, the urethra as the center of the sex sphere and with its rich sensory nerve supply is apparently the most frequent offender. The following facts are listed as supportive evidence of the outline theory:

1. The previously mentioned failure of many investigators to find a direct relationship between menopausal symptoms and the hormone levels in the blood and urine.

2. The striking similarity between menopausal symptoms and the symptoms of prostatism. Emphasized in particular are the symptoms of local urethral irritation such as urgency, frequency, dysuria and stress incontinence.

3. The frequent onset and aggravation of rheumatic symptoms in the menopause.

4. The fact that many women with typical menopausal symptoms who do not respond to treatment with estrogens are relieved by local treatment of the urethra.

Diagnosis and Treatment

Most women are relieved by estrogens and sedatives. For those who are not sufficiently relieved the following procedure is suggested:

1. Treat urinary infection, if present.

2. If urine is negative, catheterize, instill ½ ounce of ¼ per cent nupercaine solution into the bladder, and pass a metal sound into the bladder for five to ten minutes. If the patient's symptoms are relieved within about a half hour, the urethra is the source of the symptoms. Unless the relief is very striking, one single test should not be relied upon.

3. If the previous test has been negative or inconclusive, cystoscopy is performed. Any gross urethral or

bladder neck pathology is corrected by fulguration. If no extensive bladder neck pathology is found, the bladder neck and posterior urethra are injected with 1 per cent novocain solution through a McCarthy needle. If the patient is relieved of her symptoms, this is proof that the symptoms were cuased by the urethra. The novocain infiltration can also be performed through the vagina, but this method is less accurate than injection through the cystoscope.

These two tests also have therapeutic value. Sounds are applied twice weekly for two to four weeks, then whenever necessary for relief of symptoms. One single novocain infiltrations has often given prolonged freedom from symptoms but usually after treatment with sounds is necessary. In some stubborn cases x-ray irradiation of the urethra has been of value. Transurethral resection of the bladder neck has given satisfactory results in women who had residual urine.

References

1. Pratt, J. P.: *Tice Practice of Medicine*, Hagerstown, Maryland, W. F. Prior Co., 1922, vol. 8, chap. 6, p. 514.

2. Wharton, L. R.: *Gynecology*, Philadelphia, W. B. Saunders Co., 1943, p. 191.

3. Curtis, A. H.: *Obstetrics and Gyneocology*, Philadelphia, W. B. Saunders Co., 1935, p. 157.

4. Novak, E.: *Lewis' Practice of Surgery*, Hagerstown, Maryland, W. F. Prior Co., 1948, vol. 11, p. 54.

5. Hock, E.: Urol. & Cutan. Rev. 53: 149 (1949)

6. Folsom, A. I., and O'Brien, H. A.: J.A.M.A. 128: 408 (1945)

7. Hock, E.: J. Urol. 57: 1069 (1947).

8. Heller, C. G., and Myers, B. B.: J.A.M.A. 126: 472. (1944)

Treatment of Fractures of the Foot

By C. F. FERCIOT, M.D.

Lincoln Orthopaedic Clinic
Lincoln, Nebraska

Adequate x-ray study of the foot must be made in all cases where fracture is suspected. Such study should include a true lateral view of the entire foot and ankle, an antero-posterior view of the forefoot, an antero-posterior view through the mid-tarsal region, an oblique view of the forefoot and tarsal area, and an antero-posterior view of the os calcis.

The hind foot is composed of the astragalus and os calcis. The astragalus is subject to fracture in falls from any height, or in automobile accidents where severe twisting stress is applied to the foot with compression force. Fracture mot commonly occurs through the neck of the bone and early reduction is important as the chief blood supply to the articular portion is carried through nutrient vessels entering via the neck of the bone. Aseptic degeneration of the articular body of the bone is prone to follow, particularly in fractures through the base of the neck that are not reduced early. An

equinus position of the forefoot with direct manipulation of fragments is frequently successful in securing reduction. Expert opinion should be sought if reduction is questionable.

Fractures of the os calcis are usually the result of fall from a height, or sudden upward forces, as in an explosion. Varying degrees of impaction and comminution are usually present. Early and adequate sedation is urged, as it lessens tissue swelling. If possible, reduction should be carried out before severe swelling develops. A low spinal block gives excellent relaxation, lessens post-traumatic swelling and is desirable in most cases of severe injury to the extremity.

The principle of complete disimpaction of the fracture, as advocated by Yoerg, is recommended. This is accomplished by strong lateral manipulation of the heel. Following this, the knee is flexed over the edge of the table and, with the foot held in plantar flexion, the heel is grasped and pulled down strongly with lateral molding of the fragments from side to side and upward under the instep. Judicious use of a heel clamp is helpful in correcting lateral displacement. The heel is padded with a single layer of felt and a snugly molded cast is applied from the toes to just below the knee. Lateral plaster splints are applied and the cast is thin anteriorly so that it can be radily split anteriorly without loss of heel position, should this become necessary. Early manipulation is urged and should not be deferred because of swelling, although judgment in the use of a heel clamp is necessary when severe swelling is present. Snugging of the plaster is carried out a soon as it loosens by removing an anterior strip. The cast is changed as often as need be to maintain a snug, well molded fit. In practice, the pull of the tendo-Achilles has not been found to be a deforming factor in these fractures when treated by this method. If x-ray recheck is satisfactory, the patient is allowed to be ambulatory on crutches within a few days and the plaster is continued for a period of six weeks. The case is re-evaluated at the end of this time and if subastragalar relationships are not satisfactory, subastragalar stabilization is recommended. In the usual case, the cast is left off at this time and motion is encouraged with the wearing of a supportive shoe; but weight bearing is deferred until the end of eight weeks, after which graduated weight bearing is encouraged with the aid of crutches. It is felt that early surgical treatment of selected cases offers a more definite assurance of satisfactory functional outcome and shortens the period of morbidity.

The bones of the mid-foot form the central portion of the arch of the foot and their fracture is frequently associated with other injuries. Fractures of the scaphoid and cuboid bones are of greatest clinical importance. Their reduction and immobilization are important to satisfactory functional outcome. Fractures of the midfoot and forefoot can frequently be made ambulatory by the use of a well fitted walking type cast.

In fractures of the metatarsal bones it is particularly important to maintain length and alignment in order that the structural components of the foot may function in a normal manner. Attention is called, however, to one instance in which this is not desirable, namely, in case of march fracture of the second metatarsal bone where this bone is

longer than normal, when a certain degree of shortening will result in a better functioning foot.

Fractures of the first and fifth metatarsal bones require particular attention and adequate functional realignment is essential. In oblique fractures, particularly of the first metatarsal, open reduction is often desirable.

Fractures involving the metatarsophalangeal joints, especially the first, are prone to be disabling and every attempt must be made to secure a good reduction and maintain protection until healing has occurred. The use of skeletal traction is often desirable on the great toe.

Fractures of the distal portion of the great toe and of the smaller toes may often be simply treated by stiffening the sole of the shoe by means of a thin steel plate in the sole.

Rehabilitation is extremely important following fractures in the foot. The judicious use of the walking cast, the use of active toe exercises, graduated return to functional activity, the avoidance of overstrain by the use of protective shoes during convalescent period, are factors in the management of these fractures which will tend to shorten morbidity and greatly improve the functional result.

Bibliography

1. Boehler, L.: *Treatment of Fractures*, 4th English Edition, 1935.

2. Cotton, F. J.: *Fractures and Dislocations*, 2nd Edition, 1924.

3. Herman, A. J.: *Bone and Joint Surg.*, 17:709, 1937.

4. Moore, J. R.: Os Calcis, *Diseases and Injuries of. The Cyclopedia of Medicine, Surgery and Specialties*, Vol. 10, 1941. F. A. Davis Co.

5. Palmer, I.: J. *Bone and Joint Surg.*, 18:566, 1936.

6. Watson-Jones: *Fractures and Joint Injuries*, 3rd Edition.

7. Wilson, Phillip D.: J.A.M.A., Vol. 89, P. 1676-82.

8. Yoerg, O. S.: Surgery, 2:493, 1937.

9. Key, J. A. Conwell, H. E., and D'Harcourt, J.: *Fracturas, Luxaciones y Esquinces*, Vol. 1 & 2, 1946.

10. Schrock, R. D., Johnson, H. F., and Waters, C. H., Jr.: *Fractures and Fracture-Dislocations of the Astragalusa* (Talus); J. *Bone and Joint Surg.*, V. 24, P. 560, 1942.

SIDE-GLANCES at HISTORY OF MEDICINE

EPIDEMIC PLEURODYNIA (BORNHOLM DISEASE)

Several authors were credited with the first description of this syndrome. W. Rimpau (Munchen med. Wchnschr. LXXXV, 1938, p. 221) states that Georg Hanneaus or Hannes in 1732 gave the first account of the disease. Many believe, however, that it was first accurately observed by J. Finsen in 1856 who reported on it as "Iagtagelser angauende sygdomsforholdene i Island. Copenhagen, 1874. The first paper in the United States was apparently published by W. C. Dabney: Account of an Epidemic Resembling Dengue, Which Occurred in and around Charlottesville and the University of Virginia in June 1888. Am. J. M. Sc. 96:488, November 1888.

Observations of the Prognosis of Diseases of the Liver

By H. J. ZIMMERMAN, M.D.

Chief, Medical Service, Veterans Administration Hospital, Omaha, Nebraska, and Assistant Professor of Medicine, University of Nebraska College of Medicine.

The intensive study of infectious hepatitis during and since World War II and the extensive use of needle biopsy of the liver during the past decade have added greatly to our knowledge of the life history of liver disease.

Death in acute hepatitis is relatively infrequent, the usual mortality rate being about 0.2%.[1] The occasional fatal outcome may represent a fulminant illness (acute yellow atrophy) or a lingering one (sub-acute yellow atrophy). Deep jaundice, nausea, vomiting, and mental changes point to a critical case.[2] The mortality rate of serim hepatatis has been considerably higher than that of acute infectious hepatitis. While survival from an acute episode of hepatitis is high, the incidence of disabling residua is relatively considerable. There has been noted prolongation of convalescence varying from relapse with eventual recovery (approximately 14%) to chronic hepatitis (3-4%). In a very small group (1% or less) distinct abnormality of liver function has been associated with persistent signs and symptoms of active liver disease. It is this group that offered a grave prognosis[3]. Negative — properly selected — liver function tests are a reasonable assurance that persistence of symptoms need not be of great concern (bromsulfalein excretion, thymol turbidity, cephalin flocculation, serum bilirubin and urine urobilinogen).

In a patient with persisting symptoms and borderline laboratory and clinical data, biopsy of the liver may have to be performed for help in diagnosis. While the precise incidence of cirrhosis as a sequel to hepatitis is still unknown, it is probably well under 1%[3]. The following figure represents the prognosis of Infectious hepatitis:

Death (0.25-0.5 percent). Rare epidemics (11-50 per cent). Direct Recovery (80-85 per cent)

The prognosis of chronic hepatitis, as has been implied, is even more uncertain than the frequency. Most patients recover as shown by the drop in incidence of those with residua from 17% at 3 months to 3% at 12 months[4]. When the diagnosis of post-necrotic cirrhosis has been established by a clinical picture including hepatomegaly, splenomegaly, gastrointestinal bleeding, spider angiomata, jaundice and impaired liver function, death from hematemesis, chlolemia or intercurrent infection may be expected within a period of a few months to 8 years.[5] The principles of treatment of acute hepatitis with emphasis on adequate bed rest and the provision

Sponsored by the VA and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

of a good diet can do much to minimize the development of sequelae. It has been suggested that a greater hazard is posed by anicteric hepatitis inasmuch as the patient without jaundice is less likely to receive opitmal treatment than the jaundiced patient who is considered more gravely ill.

Toxic hepatitis occurs after exposure to toxic materials such as arsenical, halogenated hydrocarbons, phosphorus, and the toxin of Amanita phalliodes. Death from acute yellow atrophy is frequently seen in those toxic hepatidites. Occasional cases of cirrhosis have been observed in humans after toxic hepatitis. The significance of residua in those patients recovering from acute toxic hepatitis must be judged in the same fashion as those patients receovering from acute infectious hepatitis.

The prognosis of fatty liver metamorphosis is difficult to evaluate. It occurs in diabetes mellitus, ulcerative colitis, tuberculosis, anemia, and pellagra. The significance of the hepatic changes in these diseases has been submerged in the clinical picture of the basic disease. The lesion of the liver may be significant, however; there has been recent evidence suggesting increased incidence of cirrhosis in diabetes, ulcerative colitis and pellagra. Of greater clinical importance is the fatty liver which develops in chronic alcoholics[6]. It should be suspected when an alcoholic has hepatomegaly with or without splenomegaly. While bromsulfalein excretion is further evidence that hepatomegaly represents disease, an enlarged fatty liver can be occasionally found in the presence of normal liver function. Acute hepatic insufficiency associated with jaundice and fatty metamorphosis and necrobiosis of cells is occasionally seen in the chronic alcoholic after a prolonged period of debauchery.

As to the prognosis of Laennec's cirrhosis Ratnoff and Patek found that more than 60% of the group had died within one year after onset of the first symptoms. Only 17% of a large group survived 2 or more years after the onset of ascites. After the development of jaundice only 23% lived two years or more. 70% of patients with hematemesis were dead within a year after the first hemorrhage. These gloomly figures were arrived at before the era of modern treatment. Most observers are agreed that a considerably improvement in prognosis can be effected by the provision of an adequate diet with or without the supplements such as lipotropic agents and vitamin and abstention from alcohol. Ascites and hematemesis can be improved by modern management. In general, the more fibrosis there is and the less fatty metamorphosis the less may be expected from treatment.

References

1. J. R. Neefe. Med. Clin. N. Am. 30: 1407. 1946.

2. B. Lucke. (a Am. J. Path. 20:471, 1944. (b) ibid. 20:575, 1944.

3. H. G. Kunkel; D. H. Labby and G. L. Hoagland. Ann. Int. Med. 27:202, 1947.

4. H. G. Kunkel and D. H. Labby. ibid. 32:433, 1947.

5. H. Kalk. Deutsche med. Wchnschr. 73:379. 1948—R. L. Fischer and M. Zuckerman. Am. J. Dig. Dis. 13:361, 1946.

6. C. L. Conner. Am. J. Path. 14:347, 1938.

A complete list of the references may be obtained by request from the editor.

Glomerulonephritis

A 7-year-old girl was admitted to the hospital with a typical acute glomerulonephritis. About one month before admission she had been ill with a virus pneumonitis and had been treated by her family physician. She recovered within two weeks. Yet, one week after recovery she suddenly had a severe hematuria. An interview with the parents revealed that three years ago the child had been treated with sulfonamides for an acute respiratory infection; she, then, showed signs of sulfa-crystallinuria with considerable edema, for a short period. The parents believed that the reaction to the sulfonamide medication was within the normal reaction range. One staff member raised the question whether the virus pneumonitis could have been a precipitating factor for the recurrence of the kidney symptoms while another member inquired about the possible connection of the previous sulfonamide crystallinuria and the present acute glomerulonephritis.

It was the opinion of one senior staff member that glomerulonephritis following virus pneumonitis is not usually seen and that more probably a coincident bacterial infection was the etiologic factor. He also contended that sulfonamide therapy would not cause glomerulonephritis but may cause a lower nephron nephrosis. On the other hand, he suggested that the child may have had a glomerulonephritis in connection with the acute respiratory infection three years before and that the recurrence of that condition could be expected with an intercurrent infection. Another physician also emphasized that sulfonamide crystallinuria would not cause a glomerulonephritis and that the kidney would neither be permanently affected nor a locus minoris resistentiae when the patient survives a severe sulfonamide crystallinuria. A third doctor stressed that the etiology of glomerulonephritis is not known except in cases of chemical poisons. Precipitating causes are: tonsillitis, scarlet fever, diphtheria, pneumonia and many other infections, also exposure to cold. While he would feel sure that the virus pneumonitis was the precipitating factor of the acute attack of glomerulonephritis he would not commit himself as to the connection with the sulfonamide crystallinuria in the previous history. A fourth staff member stated that as to his opinion the diagnosis of sulfonamide crystallinuria three years ago was not sufficiently substantiated. An acute glomerulonephritis following the minor respiratory infection could not be excluded with certainty. If the child at that time had not merely a sulfonamide crystallinuria but an attack of glomerulonephritis, the intercurrent virus pneumonia could have caused the recurrence of acute kidney symptoms. He pointed to the possibility that three years ago the condition may have been a crystallinuria plus a glomerulonephritis.

A consultant quoted the recently published book by J. F. A. McManus (Medical Diseases of the Kidney, Lea & Febiger, Philadelphia, 1950). This author points to the fact that "the allergic manifestations of sensitivity to sulfonamide in the skin and elsewhere are rarely complicated by an acute renal failure." The microscopical picture of sulfonamide crystallinuria is quite distinctive. "It is worth mentioning because acute glomerulonephritis and periarteritis nodosa are said to be allergic manifestations" as is sul-

fonamide crystallinuria. On page 114 of this book the author shows a very instructive picture of a toxic nephrosis due to sulfonamide allergic reaction. There is a dense interstitial inflammation. The epithelium of the tubules is flattened and the tubular lumens are dilated. This is obviously not the usual sulfonamide nephrosis which is due to precipitation of crystals as a result of reduced urine volume; yet it appears that an allergic inflammatory reaction after sulfonamide intake also is possible.

(lit.: N. I. Nissen et al. Renal Complications and Sulfonamide Treatment. Foreign Letters, Denmark, J.A.M.A. 1:130, May 1920—A. I. Suchett—Kaye. Brit. M. J. 1: 704, March 22, 1950—A. C. Corcoran and I. H. Page. in chapter 16, p. 481 of Wm. A. Sodeman. Pathologic Physiology: Mechanism of Diseases, W. B. Saunders Company, Philadelphia, 1950—Chas. J. McGee. Am. J. Med. Sc. 218:636 December 1949).

Prolonged Labor

Question:

I am a country doctor; the nearest hospital is about 20 miles away. Which management of prolonged labor would you suggest, considering the fact that most deliveries of my patients have to take place at their country home? F.D.K., M.D. South Dakota.

Answer:

It is recommended to administer 30,000 to 100,000 units of penicillin intramuscularly when the diagnosis of prolonged labor is secured. Each day in the morning posterior pituitary extract should be injected (one minim). (Dilutions of 1:750 to 1:1500 also were used, by intravenous route, 30 drops per minute, to overcome uterine inertia). After 30 minutes again 1 to 2 minims are injected. This may be repeated in the early afternoon. For the night a sedative should be given but only when early delivery is not expected. (2cc. of a 50% solution of magnesium sulphate, one half of a grain of morphine and one hundredth grain of scopolamine). The fluid balance should be carefully watched; possible dehydration should be combatted with at least 2,5000 cc. of fluid intake daily. The psychological side of conducting labor is important in these cases. It should be remembered that the well controlled use of analgetics and anesthetic drugs to relieve pain has not produced any increase in fetal mortality. The physician's correct psychological approach to the problems of childbirth to be managed in the home of the patient is particularly essential in prolonged labor where a suggestive and balanced attitude is helpful both to the patient and her family.

Acute Benign Pericarditis

Acute benign pericarditis continues to be mistaken for especially acute myocardial infarction. Pain, precordial or substernal, occurring in a person of the precoronary age group, should suggest benign pericarditis. This is particularly true if there is a history of an antecedent respiratory infection, abnormal temperature, sweating, weakness and anxiety accompanying onset of pain. The significant diagnostic hint is exacerbation of pain on deep breathing. It is present at the outset, and this symptom means acute pericarditis or acute pleuropericarditis, not acute myocardial infarction. Abdominal pain radiation may be erroneously diagnosed, for the thoracic origin of the pain may be entirely overlooked. Shallow and rapid respirations are an early and prominent symptom. The patient is generally unable to breathe in recumbent position. A diagnostic sign is the characteristic posture: sitting or forward or lateral leaning to relieve the pain. A pericardial friction rub is the final clinical sign; it is heard early in the disease and may be audible for a short time only. It is well localized, either in the pulmonic area or immediately to the left of the lower part of the sternum. X-ray examination frequently shows an increase of the heart shadow. Pericardial effusion may be the cause in some cases. A shocklike syndrome, manifested by anxiety, ashy cyanosis, sweating, weakness, lowered blood pressure, bradycardia, nausea and vomiting was present at the onset in some degree in all patients. It was promptly relieved by parenteral administration of grain of morphine sulfate and 1/100 grain of atropine sulfate. An elevation of temperature, increase in leukocyte count and acceleration of the sedimentation rate occur with, or shortly after, the onset of pain. Serial EKGs are of utmost importance: the diagnosis of acute benign pericarditis can be made from the limb lead racings: initial elevation of the 3-T segment in one or more leads, with upright T waves; in later stages the segment may show an upward convexity, with deeply inverted 'coved' T waves as in acute myocardial infarction. The S-T segment may remain elevated for weeks but generally returns to the isoelectric line in 3 to 7 days. Treatment with aureomycin and terramycin effected rapid symptomatic improvement. Unless one follows the clinical picture closely, in conjunction with repeated EKGs, acute benign pericarditis will continue to be mistaken for myocardial infarction. (O. F. Rosenow and C. J. Cross. Arch. Int. Med. 6:795, June 1951)

Atypical Primary Pneumonia

There is a variety of clinical patterns. Cough, malaise, fever, sore throat, chilliness, anorexia, headache are the commonest symptoms. Maximal temperatures occurred on the 11th or 12th day. 79% of the patients were afebrile by the end of the third week. Physical findings corresponded with the x-ray findings in only 50% of cases. The average duration of the pulmonary findings was three weeks. Increase of leucocyte count accompanied the spread of the pulmonary lesion. Counts up to 35,000 were found to occur in the absence of secondary bacterial invasion. In 65% of cases the cold hemagglutinin and streptococcal agglutinin titers were increased fourfold or more in direct correlation to the severity of the disease. (Wm. S. Jordan. et al. Am. J. Med., January 1951).

DIAGNOSTIC SUGGESTIONS

Mesentric Vascular Occlusion

The condition usually occurs in elderly persons with some degree of polycythemia vera, intra-abdominal infections, trauma, incarcerated hernia or an ulcerating carcinoma may be the causitive factors of a thrombosis. Embolism may occur in elderly individuals with auricular fibrillation and cardiac failure; It also may follow recent coronary enfarction or any type of vegatative endocarditis. Arterial occlusion rapidly changes to gangrene while in venous occlusion the process is much slower. Venous thrombosis has a slow onset with mild to moderate colicky pain and tenderness of the lower abdomen. Low temperature with marked leukocytosis are present. In arterial occlusion the onset is sudden with violent pain. At times the involved bowel can be felt as an indefinate mass.

(J. W. Fleming, Jr., The Journal of the Missouri State Medical Assn. 7:531, July, 1951.)

Postinoculation Poliomyelitis

Poliomyelitis following inoculations of immunizing materials of various sorts, with paralysis in the inoculated limb may be due to accidental introduction into peripheral nerves of virus from the patient's own skin, or from previously contaminated needles or syringes inadequately sterilized, rather than to exacerbation and localization of preexistent infection. The onset of symptoms and paralysis has regularly occurred after an asymptomatic interval corresponding with the established incubation period of poliomyelitis; the intervals appear to be longer into the leg — greater length of nerve to be traversed by the virus; the syndrome has been produced experimentally in monkeys. (H. K. Faber. Pediatrics. 7:300 February 1921).

Virus Encephalitis

The clinical pictures of western equine and St. Louis encephalitis are not distinguishable. The incubation period is between 4 and 21 days. Prodromata are: headache, drowsiness, fever and gastrointestinal disturbances which are followed by severe headache, insomnia, vertigo, nuchal rigidity and Kernig's sign. Lethargy, speech disturbances, ataxia, nystagmus, convulsions, confusion, amnesia and occasionally coma my occur. Paralysis is observed in about 15% of cases, usually of the spastic type. Ophthalmopegia and ptosis are rare and are seen in the equine variety. Recovery is complete in the majority of cases, yet there may be residuals such as parkinsonism, hydrocephalus, epileptiform convulsions and mental retardation; these sequelae occur in less than 5% of cases. Definite diagnosis of both types of virus encephalitis depends on the neutralization and complement fixation tests. In the former a rising titer is diagnostically significant. The complement fixation test is more satisfactory. (I. Dravin and W. C. Dine. Ann. Int. Med. 34: 705, March 1951).

Metabolic Craniopathy

This syndrome, frequently referred to as Morgangni-Morel syndrome, is probably due to endocrine (pituitary) disturbance. It occurs most commonly in females of middle age or older, who show obesity and hirsutism and complain of headache. Other signs and symptoms are: hypertension, menstrual disturbances, weakness, focal signs of the cranial nerves, some intellectual impairment, and roentgenologic changes in the skull. The author reports on a case in which diabetes insipidus was a complicating factor. (S. Dann. Ann. Int. Med. 34:163, January 1951).

Infantile Cortical Hyperostosis

A rare disease in children; since the first report by Caffey in 1945, 37 cases have been reported. Clinical picture presents a moon faced infant from 4 weeks to 12 months of age with fever, hyperirritability, anemia, and up-set feeding habits; leukocytosis, increased sedementation rate and elevated alkaline phosphates are also present. The moon faced appearance is due to brawny edema of the mandibular region and enlargement of the mandible. X-ray appearance is characteristic and gives the best basis for early diagnosis. Sub-periosteal proliferation of the mandible, ribs, clavicle, scapulae, and long bones are typical. In the differential diagnosis scurvy, osteomyelitis, syphilitic periostitis and vitamin A poisoning have to be considered. The disase generally runs a benign course.

(C. A. Racely; J. B. Bilderback and W. Y. Burton. Northwest Medicine, 6:418, June, 1951.)

Sheehan's Syndrome

In 1937 H. L. Sheehan (J. Path. & Bact. 45:189, July 1937) described post-partum necrosis of the anterior pituitary. The symptoms and signs resemble those of Simmond's disease. The authors describe a case. They state that according to Sheehan the commonest cause is ischemic necrois of the anterior pituitary following postpartum hemorrhage and collapse. Sheehan (Quart. J. Med. 8:277, October 1939) estimated the incidence in Great Britain to be approximately two severe and seven mild cases per 10,000 population. The clinical signs may develop over long periods of time. In severe cases there may be amenorrhea and loss of libido following difficult delivery. In milder cases, bodily hair may be lost, a myxedematous appearance may develop, the breasts may decrease in size, teeth may be lost, blood pressure may become low, the BMR may be subnormal, the vagina may become small and the uterus also will decrease in size. Later, Addisonian crisis may develop with hypoglycemia and, occasionally, with secondary convulsions. The authors stress that in women who had difficult deliveries and who have symptoms such as amenorrhea, myxedema, adrenocortical deficiency, hypoglycemia, and convulsions, postpartum necrosis of the adenohypophysis should be considered in the differential diagnosis. (E. C. Clark; M. Franklin, and A. L. Sahs. Arch. Nurol. and Psychiat. 6:724, June 1951).

Familial Hemolytic Jaundice

There are two etiological theories: either a hereditary defect in the erythrocytes and in their formation, or a pathologic phagocytic action in the spleen. The syndrome usually starts during youth or early adult life. There are two forms: the latent and the chronic form, either of which may be suddenly transformed into an acute phase by occurrence of a hemolytic crisis, accompanied by pain in the upper abdomen, fever, nausea, vomiting, rapidly enlarging tender spleen, a rapidly declining number of erythrocytes and progressive jaundice. Main laboratory findings are: erythromicrospherocytosis, reticulocytosis, increased fragility of erythrocytes to hyptonic saline solution, urobilinuria, positive result to indirect van der Bergh test. Splenectomy is the treatment of choice; no blood transfusion should be given before operation. (J.H. DeWeerd; J. H. Pratt and A. B. Hagedorn. Proc. Staff Meet., Mayo Clinic, 12:335, June 7, 1950).

DIAGNOSTIC SUGGESTIONS

Polyarteritis Nodosa

Main symptoms: pain in chest, head, extremities and abdomen; main signs: fever, edema, tachycardia. Laboratory findings: increased sedimentation rate and leukocytosis. Late sign: dyspnea. Incidence shows a predominance in males between ages 40 and 50. In the cardiovascular system, enlargement of left ventricle, necrotizing lesions of the coronary arteries, infarction and fibrosis of the heart muscle are encountered; in the gastrointestinal system, enlargement of the liver and vascular involvement in pancreas, spleen, liver and mesentery are found; in the urinary system, albuminuria with casts, leukocytes and red blood cells in urine, renal arteriolar changes, glomerulonephritis occur; in the nervous many different peripheral and central signs may be found. (G. C. Griffith and I. L. Vural. Circulation, 3:491, 1951)

Benign Intraductal Papilloma

Review of 353 cases. The ages ranged between 19 and 82 years. A nipple discharge was the most frequent symptom. A sanguineous or serous discharge occurred in 78 cases. This signs is characteristic for central lesions. In occasional instances retraction of the nipple as well as dimpling of the overlying skin was observed. Pain was noted only in 2 patients. "One of the clinical features . . . that weighs strongly in favor of the benign nature of the lesion is its long duration. . . In 11 cases the symptoms had been present for 10 years or more, and in 8 other patients for five years or more. (C. D. Haagensen; A. P. Stout and J. S. Phillips. Annals of Surgery, 33: 18, January 1951).

Diverticulitis

This disease is rather infrequent. Four complications are significant: 1) perforation of the bowel; 2) fistual formation; 3) abscess formation; 4) intestinal obstruction. Diverticulitis should be considered when a patient has one or more attacks of pain in the lower left abdominal quadrant, fever, constipation, nausea (?), and occasionally some diarrhea with traces of blood. In the differential diagnosis, the following syndromes are important: acute appendicitis, carcinoma of the sigmoid flexure, tumor in pelvis and inflammatory processes. (J. D. Enderline. G. P. 3:35, April 1951).

Weil's Disease (Leptospirosis)

Noguchi, in 1917, classified the causitive organism as leptospira icterohemorrhagiae. Rats are known to carry the organisms in the kidney and excrete them in the urine. Soil, food and water, contaminated with rat urine, may become a source of infection. Dogs may also act as factors for Weil's Disease. The authors report on cases in children. The main findings were fever, headache, epigastric pain, muscular pain, prevalently in the legs and hepatomegaly with tenderness. The diagnosis was ascertained by (1) dark field examination of the blood; (2) rising titer of blood serum agglutinations; (3) positive blood culture; (4) positive guinea pig inoculations. The disease is more severe in adults than in children. There was only one death in this group; the cause of death was gastro intestinal hemorrhage. Chloromycetin was tried with encouraging results. (E. Munoz and E. Mirabol — Boletin de la Asociacion Medica de Puerto Rico — 4:219, April, 1951).

Multiple Sclerosis

Author stresses that no satisfactory treatment exists, yet much can be achieved in a symptomatic and palliative way. Stress situations (injuries, pregnancy, infections, malnutrition, exposure) should be avoided. The patient should refrain from alcohol. According to the signs and symptoms the following drugs are recommended: for relaxation of voluntary musculature, myanesin, orally, 250 mg. 6 to 9 times daily—quinine sulfate, orally, 5 gr. t.i.d. — tubo-curare, intramuscularly — prostigmine sulfate, by mouth, 15 mg. 3 to 9 times daily or 0.5 mg, intramuscularly, t.i.d.; for dilatation of peripheral circulation, histamine, 2.75 mg. intravenously daily—nicotinic acid, 50 mg. by mouth. t.i.d. —Etamon, 400 mg. intramuscularly, twice daily—Tetrathion, 0.6 mg. intravenously, once a week. For allergic reactions. histamine (s. above)—Benadryl, Pyribenzamine or Hystadyl, by mouth, 50 mg. twice daily. Vitamins: Thiamine chloride, 10 mg. by mouth, four times daily —Vitamin B_{12} 10 to 12 mg. intramuscularly, twice weekly—Vitamin E, 50 mg. by mouth t.i.d.—liver extract, 10 units once a week, intramuscularly. Hormones: ACTH and Cortisone. (A. B. Baker, Wisconsin Med. J. 50:245, 1951).

Urinary Infections

Specific treatment may be based on the knowledge of effective therapeutic agents for the various urinary pathogens: B. Coli (Mandelamine, gantrisin, sulamyd, aureomycin, chloromycetin, streptomycin. The drugs of choice are the three antibiotics); E. intermedium (aureomycin); A. aerogenes aureomycin, mycetin); B. Proteus sulamyd and gantrisin; many strains also respond to streptomycin and chloromycetin); Pseudomonax aeroginosa (mandelamin and all sulfonamides); Alkaligenes gantrisin and aureomycin); Streptococcus fecalis (Mandelamine, sulfamyd, aureomycin and chloromycetin); Streptococcus hemolyticus both alpha and beta hemolytic streptococci are senstivie to penicillin, aureomycin and chloromycetin); Streptococcus nonhemolyticus (penicillin); Streptococcus aureus (Penicillin, also mandelamine, sulfonamide mixtures, aureomycin and chloromycetin). R. H. Cummings. Arizona Medicine. 7:28, July 1951)

Chorea Minor

Epstein's classification of chorea seems to be particularly appropriate for clinical differentiation. He distinguished between infectious or pathologic chorea, functional or physiologic chorea and psychologic or affective chorea. Author treated 21 cases belonging to the infectious type. He treated the patients two or three times daily with 3 to 7 units of insulin and, at the same time, administered sugar orally together with a diet rich in carbohydrates. The results were promptly satisfactory in 20 cases. Girls reacted more quickly than boys, probably because of endocrine reasons. The author's theory is that endocrine factors are involved in the pathogenesis of chorea and that insulin as a hormone influences the other endocrine centers and also the autonomic nervous system. By inhibition of the central regulations and coordination of the muscular innervation in chorea, an improvement could be accomplished. Author's material is not large enough to permit final conclusions. (E. Mayerfofer. Annales paediatrici, 176:297, May 1951).

THERAPEUTIC SUGGESTIONS

Asymptomatic Neurosyphilis

The immediate results of treatment with 4,800,000 units of penicillin in 112 patients having asymptomatic neurosyphilis with active spinal fluid findings are evaluated on the basis of the spinal fluid cell count. 10 patients (about 8.9%) failed to attain a normal cell count at the end of 6 months or showed an initial response, followed by a rise in cells later on. Most failures (8 of the 10 cases) were detected during the first year of post-treatment observation. Penicillin therapy appears superior to any other form of treatment; however, the minimum dosage should be not less than 5,000,000 and, preferably, 9,000,000 units, given over a period of 10 days. It is essential to follow-up, by checking the cerebrospinal fluid cell count. Signs and symptoms of degenerative symptomatic neurosypholis may perhaps appear in those patients having minimal but undetected parenchymatous involvement at the time of treatment, in spite of good response in the spinal fluid. (W. T. Ford; R. H. Wiggall and J. H. Stokes. Arch. Int. Med. 2:225, August, 1951).

Dicumarol

There is hardly any significant difference in the velocity with which hypothrombinemia develops after oral and intravenous administration of dicumarol. Injections of dicumarol are therefore not indicated as an initial treatment. Preparations for injections can, however, be of practical value in some instances in which vomiting preclude oral administration or when diarrhea develops with consequent reduced and erratic absorption from the digestive tract. (Chr. J. Bjerkelund. The Skandinavian J. of Clin. and Lab. Investigation, 2: 115, 1951).

Petit Mal Epilepsy

Milontin (Parke Davis & Co.), N-methyl-a-phenylsuccininde, has been found equal or to surpass trimethadione (tridione) in therapeutic efficacy and is relatively nontoxic. The average daily dosage was 2.4 gm. in units of 0.3 gm. capsules or 8 capsules daily. The range of the effective dosage varies. The maximal daily dose given with no ill effects was 4 gm. in one case. The usual practice was to begin with 0.3 gm. t.i.d. and increase the dose by 0.3 or 0.6 gm. each week until the average daily dose of 2.4 gm. was reached. Toxic signs appeared in 22% of the cases treated: nausea, dizziness, drowsiness, vomiting, headache, dreamlike states. Complete control of seizures was obtained for a period of from 4 to 31 weeks, with an average of 12 weeks for the group treated. Practical control was secured in 30% of the cases; 32% showed an average reduction of attacks of 50%, while 8% of the cases were not helped. (Frederic T. Zimmerman. Arch. Neurol. & Psychiat. 2:156, August 1951).

Parkinson's Disease

Only a return to 25 to 35% of the normal healthy state has been achieved by the many medical and surgical techniques in use. McColluch and Lettvin recently found that subemetic doses of apomorphine hydrochloride relieved considerably both the rigidity and the tremor. According to the author, apomorphine reduces the blood pressure and also rigidity and tremor. Doses of apomorphine hydrochloride: 0.3 mg. plus atropin as subcutaneous injection. (R. S. Schwab. Boston Soc. of Psychiatry and Neurology. Reg. Meeting, Dec. 7, 1951, quoted in Arch. Neurol. & Psychiat. 2:240, August, 1951.)

Marisone

Marisone is a natural steroid complex, substantially estrogen-free, derived from pregnant mares' urine which is useful in attaining increased pulmonary vital capacities in patients with severe, intractable brochial asthma. The drug does not prevent further attacks, but mitigates them; it is nontoxic, has no untoward side-effects and is well tolerated for long periods of administration. (S. H. Jacobs and A. D. Spielman. Ann. Allergy, 3:308, May-June 1951).

Chronic Tuberculous Meningitis

The interesting point is stressed that streptomicin therapy has not only changed the clinical picture of acute tuberculous meinigitis and its prognosis but that it has created a syndrome, hitherto unknown: chronic tuberculous meningitis. After streptomicin treatment atypical signs such as transverse lesions, transitory hemiparesis, extrapyramidal reactions, hemianopsias, aphasic periods and psychotic pictures may appear. The acute psychotic reactions may even turn into chronic psychoses. In more than half of these cases treated in the acute stage with streptomycin, the development of a chronic progressive hydrocephalus has been observed. (P. Bunger and W. Geiger. Deutsche med. Wchnschr., 75:1579, November 1950).

Weber-Christian Disease

(Relapsing Panniculitis).

Characteristic is the appearance of nodular masses of fat in the subcutaneous tissue. These areas vary in size from 1 cm, in diameter to several inches; they may be painless or tender. The development is gradual. They are firm, movable and may be adherent to the skin; when they age they tend to show a central softening (dimpling). The nodules may disappear spontaneously or may persist. The nodules are distributed over a wide area, mainly abdomen, breasts, thighs, pectoral regions and arms. They do not become suppurative but may become necrotic. The occurrence of nodules is accompanied by fever associated with anorexia, malaise and muscle pains. Remissions are the rule; the intervals between the attacks may be short or last several years. Females show a more frequent incidence than males. Overweight seems to be a predisposition. Laboratory tests are generally within normal limits. Biopsy of the nodules show an infiltration of the fat with large number of lymphocytes, monocytes, and occasional leukocytes; the process is limited to the panniculus. Most fatal cases reported showed intercurrent diseases as causes of death. There is no specific treatment. The disease was described first by V. Pfeiffer in 1892; Weber in 1925 and Christian in 1928 gave extensive reports. (C. R. Shuman. Arch. Int. Med. 5:669, May 1951).

Ventricular Tachycardia

In contradiction to the general opinion that in ventricular tachycardia digitalis is contraindicated authors have administered digitalis in 3 of these cases. "It is not assumed that the digitalis in these instances stopped the tachycardia, but its use, along with other supportive measures, was followed by marked clinical improvement and the cessation of ventricular tachycardia." (J. S. Gilson and F. R. Schemm. Circulation, 2:278, August 1950.)

THERAPEUTIC SUGGESTIONS

Digitalis

The cardiac glycosides have a specific action on the myocardium. The mechanism of action is to shorten muscle fibers and to cause the heart muscle to contract more forcefully. Cardiac slowing is brought about by vagal and extravagal mechanisms. The diuretic effect is secondary to improved heart function. Indications are: congestive heart failure, either in acute stage such as pulmonary edema, or in chronic forms and also certain irregularities of the heart rhythm. It may be used in myocardial infarction when heart failure occurs early or late; it also may be applied to stop auricular premature contractions and in auricular fibrillation; it is the drug of choice in auricular flutter. (J. B. Arnold, Arizona Medicine, &; 36, July, 1951).

Phyatromine

A stabilized solution of physostigmine salicylate and atropine sulphate is an excellent medication for relief in muscle spasm in occupational injuries such as spasms, back, neck and shoulder strains, pulled ligaments and similar injuries in which there is a skeletal muscle spasm. It also alleviates pain and improves the range of motion of the affected part, thus, enabling the injured to return to work earlier. It can take the place of physiotherapy in many cases. It is as beneficial in relieving backache as is infiltrating procaine solution and is also helpful in arthritic conditions. It is manufactured by Kramer-Urban Company, Milwaukee, Wisconsin. (A. H. Stahmer, Industrial Medicine and Surgery, 7:337, July, 1947).

Addison's Disease

Extract of licorice has been used in Europe for a long time to disguise the taste of drugs and is also in use as a sweet for children. Borst demonstrated that extracts of licorice cause sodium retention and potassium loss and as a consequence, increaseed venous pressure with increased systolic arterial pressure. A patient with Addison's Disease showed maintainance of mineral balance on the administration of 15 Gm. of licorice extract per day. Authors confirm Borst's observations that licorice extract contains a substance with a desoxycortisterone-like action. (J. Groen; H. Pelser; A. F. Willebrands and C. E. Kamminga. New England Journal of Medicine, 244:471, March 29, 1951).

Banthine Bromide

Authors treated 1172 patients suffering from peptic ulcer with Banthine (50 mg. orally every six hours during the day, 150 mg. on retiring and 100 mg. one hour later). The results were compared with 200 control patients. Within 32 hours there is usually relief of pain; vomiting and nausea generally subside; antiacid therapy may be less necessary; working ability is increased. Contraindications to Banthine are glaucoma, pyloric obstruction, prostatic hyperplasia. Side-effects: increase of heartburn in a great number of cases, difficulty in voiding and elimination, or, on the other hand, incontinence. (G. McHardy; D. C. Browne; E. Edwards; F. Marek and S. Ward. New Orleans Med. & Surg. J. 103:580, 1951).

BOOKS RECEIVED

Immunology
By Noble Pierce Sherwood, Ph. D., M.D. St. Louis. The C. V. Mosby Company, 1951, Third Ed. 731 pages, Cloth.

Industrial Nutrition
By Magnus Pyke B.Sc., Ph.B. London. MacDonald and Evans, 1950. 250 p. Cloth.

Growth and Development of Children
By Ernest H. Watson, M.D. and George H. Lowrey, M.D. The Year Book Publishers, Inc. Chicago, 1951. 260 pages. Cloth.

Surgical Forum
Proceedings of the Forum Sessions. Thirty Sixth Clinical Congress of the American College of Surgeons. Boston, Mass. October 1950. W. B. Saunders Company, Philadelphia-London, 1951. 665 pages, Cloth.

Psychosurgery
In the Treatment of Mental Disorders and Intractable Pain. By Walter Freeman, M.D. and James W. Watt, M.D. 2nd ed. Charles C. Thomas, Publisher. Springfield, Illinois, 1950, 598 pages, Cloth.

Fundamentals of Clinical Fluoroscopy
With Essentials of Roentgen Interpretation. By Charles B. Storch, M.D. Grune & Stratton. New York, 1951. 196 pages, Cloth.

Postgraduate Gastroeneterology
Ed. by Henry L. Bockus, M.D. W. B. Saunders Company, Philadelphia-London, 1950. 670 pages. Cloth.

An Atlas for the Clinical Use of MMPI
By Stake R. Hathaway and Paul E. Moehl. The University of Minnesota Press, Minneapolis, Minn., 1951. 799 pages. Cloth.

Electroencephalohraphy in Clinical Practice
By Robert S. Schwab. W. B. Saunders Company, Philadelphia-London, 1951. 195 pages. Cloth.

Visual Anatomy of Head and Neck
By Sidney M. Freidman, M.D. Charles C. Thomas, Publisher, Springfield, Illinois, 1950, 217 pages, Cloth.

Physiology of the Eye
Clinical Application. By Francis Heed Adler, M.D. The C. V. Mosby Company, St. Louis, 1951. 709 pages. Cloth.

University of Pennsylvania
Thirty-Second Report of the Henry Phipps Institute for the Study, Treatment and Prevention of Tuberculosis. 1947, 1948, 1949. Henry Phipps Institute, 1950. 542 pages. Cloth.

Clinical Therapeutic Radiology
U. V. Portmann, Editor. Thomas Nelson & Sons. Edinburgh, New York, Toronto, 1950. 748 pages. Cloth.

Handbook of Medical Management.
Second Edition. By Milton Cratton, M.D.; Shelsdon Margen, M.D., and H. D. Brainerd, M.D. University Medical Publishers, Palo Alto, California. 1951. 507 pages. Paper.

Emotional Factors in Cardiovascular Disease.
By Edward Weiss, M.D. Charles C. Thomas Publisher, Springfield, Illinois. 1951. 64 pages. Cloth.

Treatment of the Nephrotic Syndrome.
By Lee E. Farr, M.D., Charles C. Thomas Publisher, Springfield, Illinois. 1951. 61 pages. Cloth. $1.75.

Anatomy of the Nervous System.
By Olof Larsell, Ph.D. Second Edition. Appleton-Century-Crofts, Inc. New York, 1951. 520 pages. Cloth.

Congenital Heart Disease.
Second Edition. By J. W. Brown, M.D. Staples Press, Inc. London and New York. 1950. 344 pages. Cloth. $6.

Cornell Conference on Therapy.
Vol. IV. Edited by Harry Gold, M.D. et al. New York. The Macmillan Company. 1951. 342 pages. Cloth. $3.50.

The Growth of Physical Science.
By the late Sir James Jeans. Cambridge. At the University Press. New York. Second Edition. 1951. 364 pages. Cloth. $3.75.

Annual Review of Medicine.
Volume 2. ed. Windsor C. Cutting. Annual Reviews, Inc. Stanford, California. 1951. 485 pages. Cloth. $6.

Books on Ophthalmology

An excellent presentation of ocular physiology in its relation to the clinic[1] familiarizes the reader with all recent findings of physiology of the eye and their clinical application. In 22 chapters, with many artistic illustrations, a complete survey is given which will prove to be of great benefit for every practitioner. An extensive work on vernal conjunctivitis[2] is set forth by Dr. Beigelman. While the incidence of vernal conjunctivitis is relatively considerable in proportion to all observed cases of conjunctivitis and while the general practitioner should acquaint himself with symptomatology and treatment, this book in its special comprehensiveness is essentially a reference work for the ophthalmologist. The same holds true for the very interesting presentation on binocular vision[3] whose thorough approach affords a profound insight in this stimulating problem. On the other hand the small volume on ocular toxoplasmosis[4] is of great practical importance considering the fact that toxoplasmosis is receiving more and more diagnostic attention both in infants and adults. Thus a knowledge of the ocular manifestations is an important factor in diagnostic approach.

1. Physiology of the Eye. Clinical Application. By Francis Heed Adler, M.D. The C. V. Mosby Company, St. Louis. 1950. 709 pages. Cloth. $12.00.

2. Vernal Conjunctivitis. By M. N. Belgelman, M.D. University of Southern California Press. Los Angeles. 1950. 430 pages. Cloth.

3. Binocular Vision. By Kenneth N. Ogle, Ph.D. W. B. Saunders Company. Philadelphia & London. 1950. 345 pages. Cloth.

4. Ocular Toxoplasmosis. By Michael J. Hogan. M.D. Published for the American Ophthalmological Society by Columbia University Press. New York. 1951. 86 pages. Cloth. $2.75.

Two Books on Pathology

The second edition of the well known textbook of pathology[1] by Moore might be called with justification a classical presentation of this subject. It is not essentially a morphological but a dynamic and functional exposition and thus builds up pathology as a structural and determining foundation of clinical medicine. A very interesting and stimulating work are the studies in pathology presented to the eminent Australian pathologist P. MacCallum by his students and collaborators.[2] The 22 papers prepared by 23 authors (20 Australian, 2 British and one American pathologists) present views on many essential pathological problems and are distinguished by a great number of excellent illustrations.

1. A Textbook of Pathology. Second Edition. Pathologic Anatomy in Relation to the Causes, Pathogenesis, and Clinical Manifestations of Disease. By Robert Allan Moore. W. B. Saunders Company, Philadelphia and London 1951. 1048 pages. Cloth. $12.50.

2. Studies in Pathology Presented to Peter MacCallum. Edited by E. S. J. King, T. E. Lowe and L. B. Cox. Melbourne. At the University Press. 1950 (Cambridge University Press, American Branch, New York). 350 pages. Cloth. No price indicated.

Books On Surgery

There are hardly any more important problems the general practitioner has to face in his daily work than fractures, dislocations, and sprains.[1] The fifth edition of Key's and Conwell's reputed book presents all phases of diagnosis and management; the many and instructive illustrations intensify the didactic value of this volume. Chloroform as an anesthetic has been largely discarded; Dr. Waters and his collaborators[2] were not satisfied with this disuse and reinvestigated the properties of chloroform. They came to the conclusion that it is the most potent of all anesthetics administered by inhalation, and that it does not deserve to be abandoned as a surgical anesthetic. "However, its relatively nonirritant effects . . . upon the reflexes which inhibit breathing and prevent the inhalation of sudden high concentrations, puts it in a class with cyclopropane where the responsibility for overdose rests entirely upon the administrator." Another surgical problem the general practitioner is confronted with very frequently is differential diagnosis of the "acute abdomen"[3]. That Cope now has already published the tenth edition since 1921 proves the high practical importance of this presentation. In 19 chapters all essential aspects are concisely demonstrated.

References

1. The Management of Fractures, *Dislocations and Sprains*, by John A. Key, M.D. and H. Eraly Conwell, M.D. Fifth Edition. The C. V. Mosby Company, St. Louis, 1951, 1232 pages. Cloth. $16.

2. Chloroform. *A Study After 100 Years*, ed. by Ralph Waters. University of Wisconsin Press. 1951. 138 pages. Cloth. $2.75.

3. *The Early Diagnosis of the Acute Abdomen* by Zachary Cope, M.D. Tenth Edition. Oxford University Press. London-New York 1951. 270 pages. Cloth $3.50.

SEND FOR THIS LITERATURE

1. **Allergies** (colds)—new antihistamine
2. **Dietary deficiencies**—daily vitamin supply
3. **Respiratory infections**—penicillin inhalation
4. **Psoriasis**—oral drug
5. **Bronchial asthma**—sustained management
6. **Respiratory stimulant**—for the newborn
7. **Cough**—antitussive syrup and tablets
8. **Sulfonamide** — triple sulfa combination
9. **Rheumatic fever**—management
10. **Antihistamines**
11. **Functional Uterine Bleeding** — management
12. **Pain control**—saddle block and higher spinal analgesia
13. **Whooping cough**—relief
14. **Premature labor** — habitual and threatened abortion—management
15. **Congestive heart failure**—mercurial diuretic
16. **Birth control**—diaphragm and jelly
17. **Sore throat**—alkaline germicidal solution
18. **Cough**—management
19. **Acute bronchitis**—treatment
20. **Inflammatory glandular swelling**—topical decongestive treatment
21. **Insomnia**—gentle sedation
22. **Appetite**—tonic
23. **Functional amenorrhea** — management
24. **Peptic ulcer**—demulcent
25. **Postoperative abdominal distention** and urinary retention — prevention and management
26. **Hemorrhoids**—relief of pain and inflammation
27. **Skin affections**—therapy
28. **Gastric neurosis,** pyloris spasm, nausea—management
29. **Sedative**—without habit formation
30. **Arthralgia** (bursitis), lumbago—ointment
31. **Pregnancy test**
32. **Allergies**—management
33. **Bronchial asthma**—prolonged relief
34. **Infant feeding**—milk-free formula in allergic reactions
35. **Infant nutrition**—information
36. **Cough**—palatable creosote preparation
37. **Eye hygiene**—decongestive lotion
38. **Headache,** neuralgia—pain relief
39. **Obesity**—dietary management
40. **Arthritis**—colloidal gold sulfide therapy
41. **Trichomoniasis,** moniliasis—vaginal suppositories
42. **Asthma**—symptomatic relief
43. **Pruritus**—management
44. **Cardiovascular disorders** — management
45. **Blood sugar**—12 minute test
46. **Urinalysis**—1 minute test
47. **Gout, Gouty Arthritis**—specific therapy

Use Postage Free Card for Ordering Free Literature

NEW PRODUCTS

Neocylate with Colchicine. Neocylate contains salicylate-pabavitamin C. The formula is: Sodium salicylate 0.25 Gm. Para-aminobenzoic Acid 0.25 Gm., Ascorbic Acid. 20 mg. Colchicine). 25 mg.
Indication: gout.
Central Pharmacal Company, Seymour, Ind.

Cortical Hormones B and F. Partial synthesis of two adrenal hormones closely related to cortisone was announced by Dr. Richard S. Schreiber, Research Director. Compound F (11-desoxy-17-hydroxycortcosterone) has proved to be more active than cortisone in animal experiments. Compound B (corticosterone) is still largely untested clinically. Both compounds are now being tested.
The Upjohn Company. Kalamazoo, Michigan

Semvimin Perles. Each perle contains Vitamin A, Vitamin D, the B Vitamins, Dicalcium phosphate, ferrous sulfate, potassium iodide, manganese sulfate, cobalt sulfate, sodium molybdate, zinc sulfate, copper sulfate, potassium sulfate and Vitamin E.
The S. E. Massengill Company. Bristol, Tennessee.

Aerosporin. Active Constituents: Polymyxin B Sulfate.
Indications: Oral — bacillary dysentery, particularly the chronic type, due to Shigella and other gram-negative organisms. Parenteral — septicemia, meningitis, urinary tract and other systemic infections due to Ps. aeruginosa and some other gram-negative bacteria.
Burroughs Wellcome & Co., Inc., Tuckahoe, N. Y.

Fergon Plus. Gelatin capsules containing vitamin B_{12}, folic acid, gastric mucosa, ascorbic acid, liver fraction 2 and a special preparation of ferrous gluconate.
Indications: iron deficiency anemias, megaloblastic anemias of pregnancy and infancy, macrocytic anemia of tropical and nontropical sprue.
Winthrop-Stearns, Inc. New York, N.Y.

Phenurone (Phenacemide). Phenacetylcarbamide.
Indication: Anticonvulsant; particularly effective in treatment of psychomotor seizures; in grand mal seizures the effect was more marked when the seizures occurred in patients who also had petit mal seizures than in those who had grand mal seizures alone. As Phenurone may produce side effects on liver and blood as well as on behavior it should be tried when other anticonvulsant drugs have proved to be ineffective.
Abbott Laboratories, North Chicago, Ill.

Thysal. Each tablet contains Physostigmine Salicylate 1 mg., Homatropine Methylbromide 2 mg.
Each cc. contains: Physostigmine Salicylate 1 mg., Homatropine Methylbromide 2 mg. in a buffered solution of sodium bisulfite 0.1% and benzyl alcohol 2%.
Indications: Muscular spasms due to Rheumatoid arthritis, bursitis, spondylitis, fibrositis, traumatic neuromuscular dysfunction; as palliative in myasthenia gravis; as adjunctive treatment in poliomyelitis.
The Central Pharmacal Company, Seymour, Indiana.